AUG 25 1928

ALLERGY NUMBER

Vol. XIII AUGUST, 1928 No. 11

The Journal of Laboratory and Clinical Medicine

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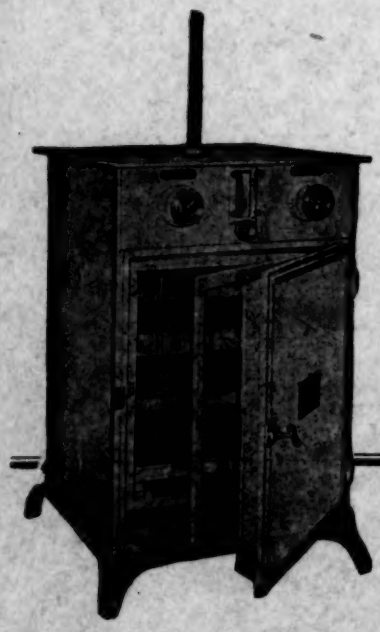

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The Journal of Laboratory and Clinical Medicine

VOL. XIII ST. LOUIS, MO., AUGUST, 1928 NO. 11

CLINICAL AND EXPERIMENTAL ALLERGY

THE VALUE OF PHOSPHORUS AND CALCIUM IN ASTHMA, HAY FEVER, AND ALLIED DISEASES*

BY ALEXANDER STERLING, M.D., PHILADELPHIA, PA.

FOR the last twenty years, theories of animal experimental anaphylaxis have been advanced by different investigators. The literature up to date is full of controversies as to the real nature responsible for anaphylaxis, especially the interpretation of its analogous occurrence in the human. In the latter it makes its appearance in different clinical entities known as allergic diseases, for instance: bronchial asthma, hay fever, angioneurotic edema, and certain skin diseases, for example: serum disease, urticaria, erythema, and eczema. Others include certain gastrointestinal disorders, some forms of cystitis, arthritis, etc.

In other words, anaphylaxis is produced in animals as a result of experimentation, and it is analogous to the so-called allergic manifestations as observed in clinical medicine. The anaphylactic phenomena are considered acquired or induced hypersensitiveness, while the above mentioned allergic diseases are thought to be due to an inherited or congenital susceptibility to hypersensitiveness.

One of the most important facts of observation in allergy is a familial tendency, its occurrence in different forms in members of the same family.

In sensitive individuals we can produce at will asthma, hay fever, eczema, etc., by direct contact, by a subcutaneous injection, by applying to a scratch on the forearm or to the mucous membrane or by oral administration of any of the offending proteins.

We can only state the facts which we observe from our experience every day, but cannot explain how sensitization does take place; possibly in utero

*From the Asthma and Hay Fever Department Samaritan Hospital, Semple University. Read before the American Association for the Study of Allergy, June 12, 1928.

through maternal or paternal inheritance. Neither can one explain why one is sensitive to animal epidermals, another to pollen and still another to food proteins, etc.

Neither can one explain with any satisfaction why the sensitivity in some patients is expressed by respiratory symptoms with the production of bronchial asthma, in others, though sensitive to the same protein, it takes the form of hay fever, angioneurotic edema, or any other form of an allergic disease.

Evidently, in addition to hypersensitiveness to protein poisons, there exists a colloidal imbalance or a chemical difference in the plasma of the cells and in the serum of the sensitized individual which not only makes him sensitive but subjects him to select sensitivity resulting in different forms of allergic diseases.

Several of the above mentioned allergies may appear in a single individual at different periods of his life, such as, eczema in early infancy, bronchitis, urticaria in youth, asthma and hay fever later in life.

Some observers explain that the occurrence of different clinical forms of allergy is due to a local deficiency in the cellular structures of the parts involved. However, the introduction of sensitivity and its recognition as an etiologic factor in asthma, hay fever, etc., is one of the most important events in annals of clinical medicine. When the offending proteins are removed, the cure or the relief obtained in 85 per cent of allergic individuals is as spectacular as the results which follow the administration of diphtheria antitoxin.

The allergy in seasonal hay fever patients can be demonstrated in 95 per cent. In perennial rhinitis patients, we get only about 25 per cent demonstrable sensitivity. In bronchial asthma we find 35 per cent to 40 per cent; other investigators invariably report from 55 per cent to 65 per cent.

In seasonal hay fever, we can obtain from 90 per cent to 95 per cent of relief. In sensitive asthmatics from 80 per cent to 85 per cent, provided that sensitivity is properly established and desensitization carefully carried out.

It was not with a feeling of disappointment when we reported to the American Society for the Study of Allergy our difficulties in desensitization.[1] It was rather to stimulate further research how to benefit the asthmatic.

A good preparation is the most important prerequisite in the proper diagnosis of sensitivity. It matters little whether one uses the dermal or the intradermal method. Many of the proteins on the market obtained for testing purposes are poor, and not enough of desensitizing material in the so-called treatment sets for hay fever.

We must not forget the fact that occasionally a patient may still be positive to something for which he was *not tested*, although covering all the routine tests on the market. For illustration, a Philadelphia druggist, an asthmatic of nine years standing, was tested and treated without any improvement. Some one advised him to go to California. He spent about eight months in Los Angeles. He was sick there just the same. When he came under my care, he was tested for pollen, animal epidermals, and foods, but he did not give any reaction. On further questioning, whether any medicine in his drug

store was responsible for his illness, he suggested that he felt worse when he compounded carroid or pappaine.

On testing with the latter two proteins, he gave the largest reaction ever seen, a wheal the size of a silver dollar with marked pseudopods extending for many more inches. He is well since he does not handle carroid and pappaine in his drug store.

As a general rule, except those who work in chemical industries, when a patient passes through the routine testing and does not show any reaction, we consider him a nonsensitive case. Others insist that one may still be sensitive to some of the proteins tested even though the tests at the time did not show any reaction.

From 55 per cent to 65 per cent of asthmatics, 5 per cent of seasonal hay fever and 70 per cent to 75 per cent of perennial rhinitis, do not show any protein hypersensitiveness on testing. They are usually considered to be due to inflammatory disturbances in the chest proper, or to follow upper respiratory infection, such as sinus involvement or any other foci of infection, teeth, tonsils, etc. When our patients fail to improve on surgical and medical treatment for the upper respiratory infection, we look for other etiologic factors; for instance, metabolic and glandular deficiencies, chronic diseases, such as tuberculosis, cardiorenal, syphilis, emphysema, etc.

Drugs, intravenous medication, stock and autogenous vaccines prepared by the Cohen-Heist or any other method, are used more or less empirically. We have related our experience with surgery of the nose and throat in asthmatics.[2] We can emphasize again the advisability for the surgeon to make a complete allergic study as well as the status of the blood calcium and phosphorus, before operative work is undertaken. Several weeks ago I had the opportunity to study a case with Dr. Nusbaum, which confirms our previous observations.

S. J., twenty-two years, an undernourished and pale girl troubled for eight years with nasal obstruction, marked sneezing and rhinitis, has severe coughing spells every three or four weeks lasting from three to five days, occasionally wheezings. She is more or less well in the summer months of June, July, and August, worse in October and November. Two and a half years ago she had a submucous resection, by another surgeon, followed by bleeding, rather severe for fifteen days until calcium chloride was given intravenously. She was very much worse after the operation; nasal obstruction more severe with constant sneezing and rhinitis. On testing she gave a reaction to duck feathers plus 2 and sheep wool plus 1. Her blood calcium 8.7 mg. per 100 c.c. of blood, blood phosphorus of 2.2 mg. I wonder if a surgeon is justified in operating in the presence of these clinical findings.

Surgical intervention and vaccine treatment cures and relieves many, but not as many as the apparent indication for their use. However, we are compelled to resort to them on many occasions. What else have we to offer our suffering patients in the absence of sensitivity, or when desensitization fails to produce desired results?

TABLE I

BLOOD CALCIUM AND PHOSPHORUS IN ASTHMATICS

NAME	AGE ASTHMA BEGAN	PRESENT AGE	ALLERGY	CALCIUM	PHOSPHORUS	CALCIUM PHOSPHORUS PRODUCT	CLINIC	RECORD
J.Mc. (M)	2½ yr.	11 yr.	Yes	10.0 mg.	D.		S.H.	Disp.
M.B. (F)	7 "	10 "	Yes	10.0 "	D.		"	"
N.F. (M)	7 mo.	9 mo.	No	10.0 "	1.15 mg.	11.50 mg.	"	"
J.M. (M)	6 yr.	24 yr.	Yes	10.0 "	1.0 "	11.0 "	"	"
M.McG. (F)	32 "	55 "	Yes	8.0 "	D.		"	"
J.B. (M)	6 mo.	6 "	No	7.0 "	1.1 "	7.7 "	"	"
B.T. (M)	40 yr.	60 "	No	11.0 "	2.2 "	24.2 "	"	"
H.K. (M)	37 "	39 "	No	8.0 "	4.0 "	32.0 "	N.L.	"
B.M. (F)	20 "	32 "	No	13.0 "	1.5 "	19.5 "	"	"
J.S. (M)	3 "	6 "	No	11.5 "	1.2 "	13.8 "	"	"
C.C. (F)	37 "	40 "	No	11.5 "	1.5 "	17.25 "	"	"
S.C. (F)	6 "	21 "	No	10.5 "	3.0 "	31.5 "	"	"
Y.C. (F)	47 "	48 "	No	12.0 "	2.7 "	32.4 "	P.C.	
F.G. (F)	24 "	32 "	?	9.0 "	1.54 "	13.86 "	"	
T.A. (M)	43 "	44 "	Yes	12.0 "	2.5 "	30.0 "	"	Dr. R-r
S.G. (M)	44 yr.	47 yr.	No	10.0 mg.	2.0 mg.	20.0 mg.	N.L.	Disp.
I.R. (M)	57 "	65 "	No	13.0 "	0.5 "	6.5 "	"	"
B.F. (M)	37 "	39 "	No	11.0 "	1.0 "	11.0 "	"	"
S.T. (M)	22 "	33 "	No	11.0 "	1.0 "	11.0 "	"	"
D.O. (M)	21 "	23 "	No	10.0 "	0.7 "	7.0 "	"	"
B.C. (M)	28 "	34 "	No	10.5 "	D.		S.H.	"
C.C. (F)	40 "	42 "	No	12.0 "	D.		P.C.	
R.W. (M)	38 "	39 "	Yes	8.0 "	3.4 "	27.2 "	"	
S.P. (F)	38 "	40 "	No	9.0 "	D.		S.H.	"
H.R. (F)	46 "	52 "	No	11.0 "	2.9 "	31.9 "	N.L.	"
H.W. (M)	10 "	12 "	Yes	10.0 "	D.		S.H.	Ward
Y.E. (F)	39 "	50 "	No	10.0 "	2.9 "	29.0 "	N.L.	Disp.
L.D. (F)	21 yr.	23 yr.	?	6.0 mg.	2.4 mg.	14.4 mg.	S.H.	Disp.
G.W. (M)	32 "	33 "	Yes	10.5 "	D.		P.C.	Dr. B-y
S.T. (M)	4 "	9 "	?	10.0 "	1.0 "	10.0 "	S.H.	Disp.
B.S. (F)	20 "	30 "	Yes	10.0 "	2.0 "	20.0 "	P.C.	Dr. S-n
J.B. (M)	60 "	66 "	No	11.5 "	4.5 "	51.75 "	N.L.	Disp.
J.H. (M)	58 "	60 "	No	11.0 "	3.1 "	34.1 "	"	"
J.P. (M)	4 "	7 "	No	9.0 "	3.0 "	27.0 "	P.C.	
B.M. (M)	34 "	42 "	Yes	10.0 "	0.5 "	5.0 "	"	
I.L. (F)	20 "	30 "	No	9.0 "	3.3 "	29.7 "	N.L.	"
J.S. (M)	5 "	14 "	Yes	10.0 "	D.		P.C.	
E.P. (F)	50 "	52 "	No	10.6 "	D.		S.H.	Ward
J. F. (M)	48 "	58 "	No	11.0 "	1.2 "	13.2 "	P.C.	Dr. G-y
M.K. (M)	32 yr.	40 yr.	?	13.0 mg.	1.1 mg.	14.3 mg.	N.L.	Disp.
D.K. (M)	31 "	38 "	?	8.0 "	2.0 "	16.0 "	"	"
G.D. (F)	22 "	23 "	No	8.0 "	3.4 "	27.2 "	P.C.	Dr. G-g
S.G. (M)	2 "	5 "	Yes	9.5 "	3.8 "	36.10 "	"	Dr. E-k
M.L. (M)	26 "	27 "	No	9.2 "	3.8 "	34.96 "	"	Dr. S-d
T.R. (M)	4 "	13 "	No	10.0 "	2.2 "	22.0 "	"	Dr. M-l
A.M. (M)	28 "	30 "	No	12.5 "	D.		S.H.	Ward
F.A. (M)	34 "	35 "	Yes	11.6 "	2.1 "	24.36 "	"	Disp.
B.H. (M)	48 "	57 "	No	9.6 "	2.9 "	27.84 "	"	"
F.R. (M)	39 "	41 "	No	10.1 "	3.5 "	35.35 "	"	"
J.W. (M)	5 "	8 "	Yes	12.6 "	2.8 "	35.28 "	P.C.	Dr. W-e
B.C. (F)	31 "	37 "	No	11.0 "	2.4 "	26.4 "	S.H.	Disp.
H.Mc. (F)	34 "	38 "	No	6.0 "	1.1 "	6.6 "	"	"
E.W. (F)	38 "	41 "	No	9.0 "	2.6 "	23.4 "	N.L.	"

D. = Deficient, below 0.5 mg.
S.H. = Samaritan Hospital
N.L. = Northern Liberties Hospital
P.C. = Private Case

TABLE II

BLOOD CALCIUM AND PHOSPHORUS IN HAY FEVER OR, POLLEN POSITIVE SEASONAL CASES

NAME	AGE HAY FEVER BEGAN	PRESENT AGE	ALLERGY	CALCIUM	PHOSPHORUS	CALCIUM PHOSPHORUS PRODUCT	CLINIC	RECORD
M.H. (M)	16 yr.	23 yr.	Yes	8.0 mg.	D.		S.H.	Disp.
J.H. (M)	12 "	28 "	"	10.0 "	D.		P.C.	Dr. M-rg
H.R. (M)	11 "	14 "	"	10.0 "	1.0 mg.	10.0 mg.	"	Dr. H-nd
I.N. (M)	39 "	44 "	"	9.0 "	2.4 "	21.6 "	N.L.	Disp.
H.W. (M)	30 "	38 "	"	7.5 "	D.		P.C.	Dr. M-ll
Dr.W. (M)	13 "	20 "	"	9.0 "	D.		S.H.	Disp.
E.K. (M)	7 "	10 "	"	10.5 "	D.		P.C.	Dr. K-s
J.C. (M)	29 "	36 "	"	10.0 "	D.		"	Dr. G-o
S.R. (F)	28 "	33 "	"	11.0 "	1.5 "	16.5 "	"	Dr. E-k
M.S. (F)	37 "	42 "	"	11.3 "	D.		S.H.	Disp.
K.T. (M)	7 yr.	13 yr.	Yes	11.0 mg.	D.		S.H.	Disp.
B.G. (F)	13 "	15 "	"	12.0 "	4.2 mg.	50.4 mg.	N.L.	"
S.Mc. (M)	15 "	47 "	"	10.9 "	1.1 "	11.99 "	P.C.	Dr. M-ll
D.W. (M)	7 "	26 "	"	11.3 "	1.1 "	12.43 "	S.H.	Disp.
B.S. (M)	27 "	32 "	"	11.0 "	1.4 "	15.4 "	"	"
J.C. (M)	33 "	36 "	"	11.0 "	1.5 "	16.5 "	"	"
E.S. (F)	4 "	5 "	"	10.0 "	3.7 "	37.0 "	P.C.	Dr. G-s
R.C. (F)	5 "	6 "	"	12.0 "	2.4 "	28.8 "	S.H.	Disp.
A.N. (F)	30 "	36 "	"	12.4 "	3.4 "	42.16 "	"	"
S.F. (F)	3 "	5 "	"	11.2 "	3.1 "	34.72 "	"	"

TABLE III

BLOOD CALCIUM AND PHOSPHORUS IN PERENNIAL RHINITIS

NAME	AGE RHINITIS BEGAN	PRESENT AGE	ALLERGY	CALCIUM	PHOSPHORUS	CALCIUM PHOSPHORUS PRODUCT	CLINIC	RECORD
R.R. (F)	29 yr.	35 yr.	No	11.0 mg.	3.3 mg.	36.3 mg.	N.L.	Disp.
S.G. (M)	24 "	34 "	"	10.4 "	2.8 "	29.12 "	P.C.	
M.C. (F)	38 "	45 "	"	5.0 "	0.5 "	2.5 "	S.H.	"
B.M. (M)	15 "	17 "	"	11.0 "	0.8 "	8.8 "	N.L.	"
L.A. (M)	46 "	57 "	"	12.0 "	2.4 "	28.8 "	"	"
S.B. (M)	28 "	30 "	Yes	13.0 "	D.		P.C.	Dr. C-n
F.H. (F)	37 "	39 "	No	9.0 "	3.5 "	31.5 "	N.L.	Disp.
E.S. (F)	20 "	21 "	"	11.2 "	3.1 "	34.72 "	P.C.	
M.K. (F)	30 "	37 "	"	11.0 "	3.5 "	38.5 "	N.L.	"
J.G. (M)	1 "	3 "	"	9.0 "	2.0 "	18.0 "	S.H.	"
J.G. (M)	12 "	13 "	"	10.0 "	2.0 "	20.0 "	"	"
S.J. (F)	14 "	22 "	Yes	8.7 "	2.2 "	19.14 "	P.C.	Dr. N-m

For many years it has been observed that allergic patients improve on the administration of calcium salts. On account of this, the theory of calcium deficiency in asthmatics was established. Study was made on patients from the Asthma and Hay Fever Department of the Samaritan Hospital, from the Chest and Asthma Clinic of the Northern Liberties Hospital, and on a number of private patients.

In this series, a study of 85 cases of blood calcium, it shows a calcium deficiency in only a small per cent; still many patients improve on calcium. In this very same group, we have made a study of blood phosphorus, and we were surprised to find a very striking phosphorus deficiency as compared with normal or high blood calcium. We see by the accompanying charts, that only twenty-three patients had a low blood calcium of 9.5 mg. or lower, while the rest, sixty-two patients, had a normal and a high normal blood calcium, rang-

TABLE IV

BLOOD PHOSPHORUS IN 85 ALLERGIC PATIENTS

a. Bronchial asthma	53	35 male	18 female
b. Hay fever	20	13 male	7 female
c. Perennial rhinitis	12	6 male	6 female
Blood phosphorus from 0.1 to 1.0 inclusive			30 patients
a. Bronchial asthma		18	
b. Hay fever		9	
c. Perennial rhinitis		3	
Blood phosphorus from 1.1 to 3.0 inclusive			38 patients
a. Bronchial asthma		26	
b. Hay fever		9	
c. Perennial rhinitis		5	
Blood phosphorus from 3.1 to 4.5 inclusive			17 patients
a. Bronchial asthma		9	
b. Hay fever		4	
c. Perennial rhinitis		4	

TABLE V

BLOOD CALCIUM IN 85 ALLERGIC PATIENTS

a. Bronchial asthma	53	35 male	18 female
b. Hay fever	20	13 male	7 female
c. Perennial rhinitis	12	6 male	6 female
Blood calcium from 5.0 to 7.0 inclusive			4 patients
a. Bronchial asthma		3	
b. Perennial rhinitis		1	
Blood calcium from 7.1 to 9.5 inclusive			19 patients
a. Bronchial asthma		12	
b. Hay fever		4	
c. Perennial rhinitis		3	
Blood calcium from 9.6 to 13 inclusive			62 patients
a. Bronchial asthma		38	
b. Hay fever		16	
c. Perennial rhinitis		8	

ing from 9.6 mg. to 13 mg. per 100 c.c. of blood. On the other hand, sixty-eight patients show a phosphorus deficiency and only seventeen have a normal blood phosphorus from 3.0 to 4.5 mg. per 100 c.c. of blood. We have observed that many patients with a low blood phosphorus make a spectacular improvement of phosphorus, especially when used in addition to any other standard form of treatment.

For illustration: a boy, ten years old, was suffering from asthma since childhood. He was undernourished, pale, and perspiring freely on the slightest exertion. While awaiting the regular routine study, he was put on phosphorus. He made an immediate improvement and was practically free from asthma ever since, which is for the past eleven months. He gained twenty to twenty-five pounds in the first three or four months of treatment. The blood calcium was 10 mg., while his blood phosphorus was too small to be determined quantitatively. Two months later his phosphorus was 2 mg., six months

TABLE VI

BLOOD CALCIUM PHOSPHORUS PRODUCT IN 85 ALLERGIC PATIENTS

a. Bronchial asthma	53	35 male	18 female
b. Hay fever	20	13 male	7 female
c. Perennial rhinitis	12	6 male	6 female

Blood calcium phosphorus product from 0.1 to 20 inclusive		51 patients
a. Bronchial asthma	31	
b. Hay fever	14	
c. Perennial rhinitis	6	
Blood calcium phosphorus product from 20.1 to 30 inclusive		16 patients
a. Bronchial asthma	12	
b. Hay fever	2	
c. Perennial rhinitis	2	
Blood calcium phosphorus product from 30.1 and above		18 patients
a. Bronchial asthma	10	
b. Hay fever	4	
c. Perennial rhinitis	4	

later 4.4 mg. This was the first case that impressed us with the study of phosphorus and the value of its use in asthmatics.

An illustration of the value of phosphorus in hay fever: A young man, twenty years of age, a dental intern, has had summer hay fever for seven years. While he was in Philadelphia, working in his hospital, he was comparatively comfortable, but at week-ends when he visited his parents on the farm, he was having severe attacks of hay fever. He was tested, found strongly positive to summer grasses, orchard grass, June grass, timothy and sweet Vernal, each plus four. The blood calcium was 9 mg.; phosphorus, too small to be determined quantitatively. He was put on phosphorus and at the same time he was requested to abstain from any other medication, and to report his experience when visiting the farm at week-ends. On his return he reported he was practically free from any hay fever attacks.

Our studies show that 66 per cent of hypersensitive and 34 per cent of the nonsensitive have a low blood phosphorus. Of the 23 cases who had a low calcium, only 7 or 30 per cent were sensitive.

All the patients, whether sensitiveness can be proved by testing or not, are put on phosphorus with variable results. In most cases the results are good.

Many of us have witnessed the asthmatic in his paroxysms, the labored breathing, the fatigue of the muscles of respiration as well as the exhaustion of the entire body. Among the students of physiologic chemistry it is known that exercise increases the excretion of phosphates. In the so-called "fatigue substances" of muscle, among other excretions the most important is potassium dihydrogen phosphate. Therefore, the state of muscle fatigue in the asthmatic may possibly be responsible for the instability or phosphorus deficiency, as observed in this series of cases.

Since our administration of phosphorus in addition to desensitization in hay fever patients, the results have been almost 100 per cent freedom from symptoms.

Young asthmatics who perspire easily on the slightest exertion, get colds often, do not perspire easily and are not subject to colds after a few weeks on phosphorus.

Calcium is beneficial in most hypersensitive cases, whether they show a low blood calcium or not. It produces a marked improvement in seasonal hay fever; in some cases of perennial rhinitis and in bronchial asthma, it stops the leaking sensitive mucous membrane of the upper respiratory system. Both calcium and phosphorus help to control the hyperexcitability of the nervous system.

The interrelationship between calcium and phosphorus metabolism has been recognized for some time, which is expressed by Howland and others "that an excess of calcium impairs phosphorus retention; excess in phosphorus is unfavorable to calcium absorption." Clinically we find calcium and phosphorus both low in some individuals; on the other hand, calcium and phosphorus both high in others.

COMMENT

Hay fever patients and pollen asthmatics under our care last fall (1927) had absolute freedom from symptoms. The results were probably due to our better knowledge in desensitization, but we think that it was due to the addition of phosphorus and calcium medication.

The mucous membrane is constantly bathed in the (circulating) blood serum which probably contains a great many defensive bodies or enzymes. The activity of the latter depends upon many unknown substances called activators. The only one known is phosphate.

In normal individuals it is quite possible that inhalants, food proteins, etc., are digested or converted by these defensive bodies when activated on by many substances as yet unknown (the only one known is phosphate). This process probably renders the protein absolutely harmless when it gets in contact with the mucous membrane of the respiratory or gastrointestinal system.

On the other hand, in the allergic patients, the inhalants, food and bacterial proteins are not being activated on; therefore, they are not destroyed or converted by the defensive body substances. Consequently the above mentioned proteins act as irritants, producing asthma, hay fever, etc.

The allergics as shown by our charts are deficient in phosphorus, some in calcium and improve when the latter two are added to the treatment. F. J. Novak, Jr., and A. R. Hollender,[3, 4] R. Sonnenschein and S. J. Pearlman,[5] F. M. Pottenger,[6] and Graftis T. Brown and Oscar B. Hunter[7] found calcium deficiencies in allergics and reported improvement in the majority of these patients upon the addition of calcium.

Therefore, are we not justified to infer that phosphorus and calcium are probably playing the rôle of activators for the defensive or enzymic activity in our blood stream, and help in the proper conversion or rendering the inhalants, bacterial and food proteins harmless when they reach the mucous membrane?

The relation of physiologic chemistry to the problem of allergy requires further investigation, with reference to phosphorus and calcium metabolism, and other blood minerals, especially the possibility of the presence of enzymic activity in the blood serum.

CONCLUSION

While we cannot draw positive conclusions from a study of the above number of cases, calcium and phosphorus are found of great benefit in the treatment of allergic diseases. This mineral deficiency in asthmatics, hay fever, and allied diseases, whether sensitivity can be proved or not, may be the missing link which makes the allergic differ from the normal. The addition of calcium, phosphorus, and other minerals, for instance, iron, sodium and potassium salts, are possibly responsible for the favorable results in this series of cases.

I wish to acknowledge my appreciation to Dr. Wm. Egbert Robertson for some suggestions in the construction of this paper, and to Dr. Clark, to Dr. Ginzburg, pathologists to the Samaritan and the Northern Liberties Hospitals respectively, for the laboratory work in the blood calcium and phosphorus.

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711 CENTRAL MEDICAL BUILDING.

A SIMPLE CHART BASED ON THE STUDY OF FOUR HUNDRED CASES WHICH ILLUSTRATES OUR PRESENT KNOWLEDGE OF ALLERGY*

By Milton B. Cohen, M.D., Cleveland, Ohio

ALTHOUGH the conception of asthma as a manifestation of human hypersensitiveness is accepted by most clinicians, in many of the individuals suffering from this disease it is still quite impossible to determine the active cause which sets up the reaction. And in some patients, even when the exciting cause is known, it is impossible either to remove it sufficiently from the patient's environment or to raise his tolerance to it to a sufficiently high level to prevent the occurrence of symptoms. Also, in a fairly large number of patients one is sure to find several in whom attacks seem to be brought on by purely nonspecific causes, such as temperature changes, nervous influences, mechanical factors, and certain infections. Thus the protean nature of asthma and the difficulties in evaluating the various factors in its etiology and treatment have led to a great deal of confusion, not only in the minds of the average physicians, but also in the minds of those working intensively with these patients. Each worker has been inclined to look at the problem from the angle of his own particular specialty. Thus we have nasal, infectious, toxemic, and neurogenic theories as well as the hypersensitive theory.

There seemed to be a need for some conception of allergy which would be scientifically correct for the present state of our knowledge and would at the same time correlate the known facts and observations. Accordingly, the accompanying chart was prepared. It suffices to classify and explain any and all symptoms occurring in any patient, and points out the principles necessary for their relief. It is interpreted as follows:

In the center, dividing it into two parts, is a long block labeled *Tolerance*. While all allergic patients will react to the substances producing their attacks, the tolerance is different in each, and may vary in the same individual from time to time.[1]

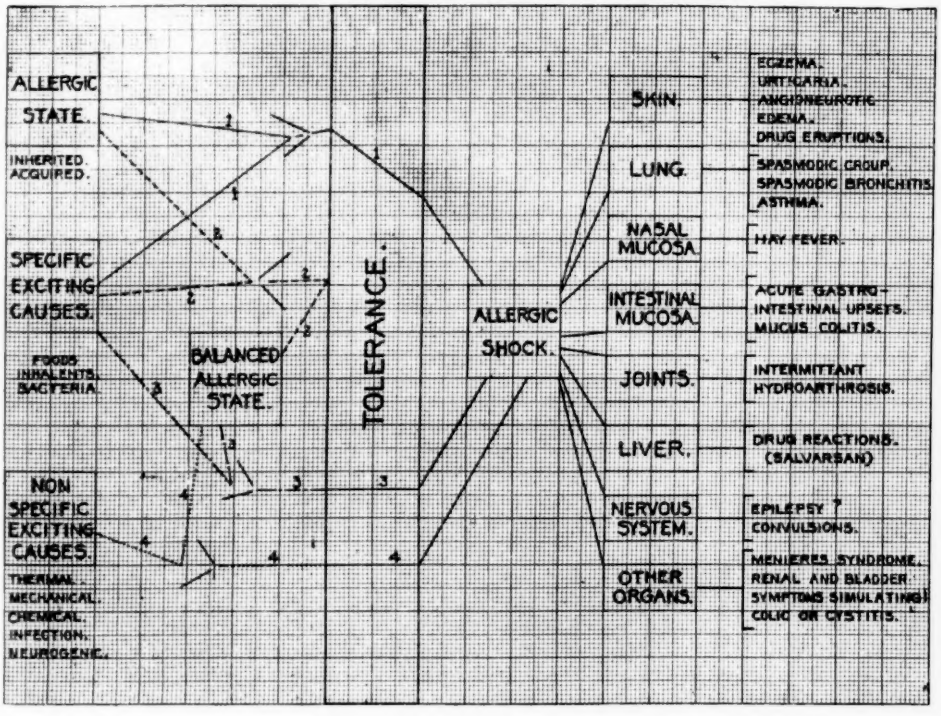
Reactions occurring on the left side of the tolerance block are symptomless; those passing beyond it to the right side of the chart are all productive of symptoms.

In the upper left-hand corner of the chart is a block labeled *The Allergic State*. This represents the hypersensitive state; patients in this state have been sensitized to some specific substance. Despite the evidence of the hereditary nature of this condition, there is evidence to believe that only the predisposition, or facility to be easily sensitized, is inherited, and that the allergic state is produced only after active sensitization by contact with the specific substance or substances after birth.[2, 3]

*From the Medical Service and the Allergy Clinic of Mt. Sinai Hospital.

Below the block representing the allergic state is a block called the *Specific Exciting Causes*. These may be foods; inhalant substances, such as animal epidermals, products of industry, molds, dusts; and bacteria. When a patient allergic to some specific cause receives a dose greater than his tolerance, allergic shock occurs, as can be seen by following Line 1. The site of the allergic reaction will depend in each case on the relative sensitivity of the different end organs of the body. These vary in their sensitivity so that in one individual there may result hay fever, in another asthma, in another skin eruptions, in another gastrointestinal symptoms, or there may be combinations of these or any other symptoms, as indicated in the blocks at the extreme right of the chart. This is the mechanism of the frank allergic reaction.

MECHANISM OF ALLERGIC SYMPTOM PRODUCTION.



Frequently, however, patients who are exposed to specific allergens constantly react periodically despite their daily exposure. During their free period these patients are in the *Balanced Allergic State*, a term coined by Dr. W. T. Vaughan.[4] This state may be produced either by a temporary raising of the level of tolerance (desensitization) or by variations in the dose of the specific substance or substances. As may be seen by following Line 2, when a patient in the allergic state receives a dose of specific allergen less than his tolerance, no symptoms result, but he is placed in the *Balanced Allergic State*. This state is particularly labile. While in it, an extra dose of some specific allergen or a reduction in tolerance may allow it to be exceeded, with a resultant allergic reaction.

At the bottom left-hand corner of the chart there is a block named *Nonspecific Exciting Causes.* Their number is legion, but they may be grouped under the headings, Thermal, Mechanical, Chemical, Infectious, Neurogenic. These have caused endless confusion in the study of allergic patients as they have frequently been considered by both patients and physicians as major causes. A very simple and common example is presented by the infant with eczema: The pediatrician attempts to adjust the diet; the dermatologist keeps irritants away from the skin; the allergist tries to remove from the patients the specific allergen. In some patients either method is sufficient; in others a combination is required. Depending on the method used to produce the healing, a different physiologic pathology is ascribed to each case. In the case relieved by ointments, etc., it is probable that the infant, in the *Balanced Allergic State*, has had symptoms produced by the additional mechanical irritation of soap, water, and scratching. The removal of these irritants afforded an opportunity for the return to the symptom-free *Balanced Allergic State.*

Another characteristic example is presented by the case of J. G., aged thirteen years, who had had attacks of asthma occurring every two or three weeks for six years. When first studied he was found to be feather sensitive, but attacks could be induced during the free interval by breathing in cold air while the chest was rubbed with ice. Feathers were removed from the home, and all attacks ceased, and have not recurred for two years. One month after beginning residence in a feather-free house, an attempt was made to induce an attack by means of cold, as described above. Despite repeated exposures, no reaction occurred. In this boy, feathers induced the *Balanced Allergic State* which, during the intervals between attacks, could be activated into allergic shock with asthma by means of a dose of a nonspecific exciting cause, cold.

The mechanism described, by which a patient passes from the *Balanced Allergic State* to allergic shock, can be followed by means of Lines 3 and 4.

From a study of this chart it will be seen at once that the treatment of allergy may be accomplished in one of two ways:

1. Remove the allergic state.

2. Reduce the doses of the specific and nonspecific causes below the patient's threshold of reaction so as to maintain him in the *Balanced Allergic State.*

The first method is impractical in most cases. In the first place, the inherited facility to acquire sensitivity is a fixed characteristic and cannot be changed. Secondly, it is extremely difficult to demonstrate beyond reasonable doubt the exact specific allergens responsible for the allergic symptoms, and it is not yet possible to obtain these in pure form. Also, patients are usually sensitive to more than one allergen. Attempts to raise the tolerance to a level comparable with that of nonsensitive individuals have been partially successful in cases with pollen disease, namely, hay fever and its accompanying asthma, but even in these the tolerance is lasting in only a small percentage. Until we have better knowledge of the exact nature of

specific allergens, and of the physical chemistry of the allergic response, removal of the allergic state is impossible, except in rare instances.

The second method of treatment, while sufficiently difficult to tax the ingenuity of the physician to the utmost, is nevertheless practical and affords relief for the large majority of patients. It is a broad clinical problem requiring the use of various special methods of study plus good common medical sense. The history of the attacks, their periodicity, their relation to specific exposures, their disappearance on change of residence or of climate, all afford clues. Skin tests with stock food and inhalant substances and with extracts of dust from the environment afford other clues. Bacteriologic study of the respiratory flora, and skin tests with these organisms give additional clues. Search for foci of infection, and for other intrinsic pathology should be made. All clues must then be subjected to careful clinical experimentation, varying one factor at a time, to determine their relationship to the patient's symptoms.

A simple outline for the study of a case of asthma is the following:

1. Remove the patient for a period of two weeks to an environment which is free of all inhalant substances. Such a condition can be produced in any room by means of a thorough renovating, covering the mattress and pillows with impervious material, and the installation of one of the electrically operated mechanical filters now on the market.[3]

2. During the stay in the dust-free room, perform routine and special skin tests, and study the effects of heat, cold, and other physical factors.

3. If the patient's symptoms disappear while in the dust-free room, attempt to correlate the symptoms with some inhalant factors in his home or working environment by actual exposure to these substances and the production of an attack.

4. Rearrange the home environment in accordance with the information gained by the above study, either by removing the offending articles of furniture, or the production of a dust-free room at home for the part-time use of the patient.

5. Arrange the diet in accordance with information obtained by the history and tests.

6. For the patients who fail to get relief by the use of these methods, attempts at specific desensitization with the bacteria to which they are sensitive should be tried.

7. Nonspecific desensitization may be of use in rare instances, and for symptomatic relief ephedrin and adrenalin are helpful.

SUMMARY

Based on the study of four hundred patients with asthma, a chart has been prepared which correlates our present knowledge of allergy, explains the mechanism of symptom production, and indicates the principles to be followed in its treatment.

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SUBNORMAL TEMPERATURE IN THE PERENNIAL ASTHMATIC PATIENT*

By William W. Duke, M.D., Kansas City, Mo.

THE temperature of a patient with asthma which is caused by sensitiveness to material things, such as pollen or hair or food, I have not found to be very interesting. There is a group, however, which does not react to anything except, as far as you can determine by history, to the effect of heat or cold or to the combined effect of the two. These patients have very severe types of asthma. Attacks can be produced by applying heat or cold in a given way and relief obtained by applying it in the reverse way. I gave a paper on this subject some time ago. I think this type of asthma is just as definite a disease as pollen disease.

I believe it is due to some damage which has been done to the heat regulating mechanism. Physicians in this line ought to recognize what a complicated mechanism the heat regulating mechanism must be. One may go to the equator and then to the north pole, and his body temperature will stay the same if he is a normal individual. Temperature is regulated largely through the constriction or dilation of the vessels and capillaries in the skin or nasal tract and bronchial tubes. Cooling takes place by radiation of the heat of the body through the skin, by evaporation of the moisture on the skin, and especially by evaporation in the bronchial tubes. Where there is little moisture on the skin and very little radiation on account of the heat in the air, cooling from the skin is not maintained and temperature is regulated almost entirely by the bronchial tree. If there were to be trouble in this heat regulating mechanism so that its work is not well done, there would be all kinds of abnormal reactions, it seems to me, in the bronchial tubes, nasal membrane, and skin. This mechanism may also partly control oxidation in the body for the generation of heat.

There are two types of individuals: one the normal, while the other reacts in a peculiar way with the production of an overstimulation in the autonomic nervous system.

In one the reaction is explosive, and rather purposeless, and in the other the reaction is inflammatory. People who are sensitive to heat and cold fall

*Read before the American Association for the Study of Allergy, Minneapolis, Minn., June 11, 1928.

into several types. The ones who are sensitive to heat alone have their illness in the summer time. The ones who are sensitive to cold alone, that is lowering of the body temperature, have their trouble in the dead of winter. There may be combined cases which may have their attacks depending upon the temperature of the outside air and their body heat, that is, the nasal membrane may be sensitive to cold air, local cold, when their body is hot, others may be sensitive to warm air when their bodies are cold, and others are sensitive to breathing of warm air or moisture when their bodies are cold. These two types are rather common and have very severe illnesses.

Another type is the one which reacts to cold air after exposure to heat, or heat after exposure to cold. Patients of this type who react to cold after exposure to heat, may exercise and get hot in the summer time and then when they sit down in the cool of a shade tree, they will react with asthma. The reverse type will, in the winter time, after they have been out and chilled by exposure to a cold temperature, come into the house, warm up, and then have an attack of asthma. In certain cases, this acts seasonally, that is a person after exposure to the cold of winter will react when the warm days of spring come along. Finally, they gain tolerance for heat and will be all right in the summer. The reverse type, the cold sensitive patient, will react in the fall, that is after they have been exposed to the heat of summer. They react to the first cold days of winter. These cases are as definite as can be. Reactions are not confined to the respiratory tract, but give all the manifestations of allergy, skin manifestations, and all.

In the regulation of body heat, the nasal mucous membrane, the bronchial mucous membrane, and the skin play an important part. If the patients belong to the allergy type of individual, their symptoms may be indistinguishable from hay fever; if they belong to the nonallergic type, the reaction comes out in a different manner, more chronic and inflammatory. The skin manifestation sometimes appear in the form of an eczema, the ugliest you have ever seen.

In one case twelve hours after exposure to heat, whether the heat of the air or exercise, the patient would develop an attack of asthma. If he kept himself quiet and cool, possibly his reactions would not be quite so great.

Heat sensitive patients usually run subnormal temperatures and usually react most severely when the temperature is inclined to be lowest.

The most extreme example I have had was a man who once had a morning temperature of 92°. It was a rule to have 94½° in the morning and 96° in the afternoon. The slightest heat would make him break out. He did not sweat. His skin was as dry as paper.

Several times we have tried intravenous peptone therapy and calcium. The temperature when stabilized very often is followed by complete relief. I think the relief which comes from peptone and calcium, and other apparent nonspecific reagents lies in modifying the action of the heat regulating mechanism. Infectious disease associated with fever will almost invariably relieve these patients for the time being. It may be that it peps up the heat regulating mechanism.

If heat sensitive patients have tonsillitis, erysipelas, or pneumonia, or as in one case, a lung abscess, they are temporarily relieved. When the temperatures come back to normal, they are more stabilized than before, and I think they may be cured of asthma for from a month to several years.

CHRONIC USE OF ADRENALIN IN THE TREATMENT OF ASTHMA*

By William W. Duke, M.D., Kansas City, Mo.

MY CHIEF reason for giving a paper on the chronic use of adrenalin is to get some discussion on the subject, and really learn something about it, because I do not feel that we are sure, by any means, that the prolonged, continuous use of adrenalin is a good thing for a person.

Everyone who has treated much asthma for any length of time, has had patients who have been taking adrenalin—four and five doses a day—for years before they came to them. I have three patients who have taken adrenalin in stupendous doses, doses amounting to as much as four ounces in twenty-four hours, two c.c. in a dose every fifteen minutes for prolonged periods of time. Patients doing that are usually in an abominable state, have a tremor, feel weak, and are very often intensely pigmented. Two of my patients have looked as though they had Addison's disease. They were as brown as that.

I do not think there is any doubt in the world but that that sort of administration of adrenalin is harmful. Whether or not the intelligent daily use of adrenalin is harmful is a question. I should certainly like to hear something pro and con on that subject.

It seems to me that it is a good idea to get a person away from adrenalin if possible, simply because it is a good idea to get a person away from any unnatural drug, especially a drug that is as potent as adrenalin.

In these patients who are taking enormous doses, the dose can be reduced greatly if one thing will be borne in mind, and that is that there are two kinds of edema in allergy, and very often in a given patient both types will be present. One is the allergic edema that gives rise to bronchial constriction in the ordinary allergy case, I mean bronchial obstruction, due to allergy. The other is mechanical edema which has nothing to do with allergy; it is simply caused by the mechanical effect of air rushing up and down the bronchial tubes, the same as it will cause edema in anyone.

I have a wonderfully instructive example of this type, a patient who had a bad pollen reaction at a time when the pollen content of the air was enormous. The man had a mild reaction; he went on a trip into the country in an automobile and had an intense exposure to weeds. He began rubbing one eye and soon came back to my office with this eye enormously swollen. The other was mildly swollen. I gave adrenalin and brought the eye which

*Read before the American Association for the Study of Allergy, Minneapolis, Minn., June 11, 1928.

was slightly swollen back to normal in a short time. The other eye remained swollen for a considerable period of time. If there is a swelling of the membranes in the bronchial tubes, is it due to allergy or is it in part mechanical? If the former, we can get relief almost always if intelligently administered. If the latter, we may get partial relief but pushing the drug to enormous dosage will not give complete relief. There is little purpose in pushing adrenalin to such doses as I have seen given in an effort to accomplish the impossible.

When we have patients who have been taking adrenalin several times a day for years, how can we get the patient away from it, and is it advisable? I found a very good substitute in the form of ten or fifteen grains of aspirin together with a good dose of whisky before the incipiency of the attack. That therapy, if it is adequately administered, is just as effective as morphine and very much less dangerous than morphine. When allergic patients become addicted to morphine, sometimes they seem to become sensitive to a lack of morphine. After that time, it is impossible to cure the asthma or the morphinism. So morphine ought to be avoided in allergy just as rat poison would be avoided. Personally, I do not use it over once a year in the case of asthma, except in patients already addicted to it. One can always get by with a large dose of whisky and aspirin. If enough whisky is given them to make them sleepy and they are made to lie down and go to sleep, that is usually the end of the attack of asthma.

If this treatment is combined with other little things we do for asthma, especially getting the patient away from the source of the trouble, or immunizing him, the dose of adrenalin can usually be reduced to a few drops at a time, maybe once or twice a night, and as a rule it is possible to get rid of it completely.

DISCUSSION

Dr. Ray M. Balycat, Oklahoma City, Okla.—Due to the redskins in the state of Oklahoma, we are either very unfortunate, or fortunate, that we are unable to use the combination that Dr. Duke referred to, that is, five grains of aspirin and a swig of whisky every fifteen minutes, but since the experience of a couple of doctors who used to live in Dallas, who now live in Leavenworth, Kansas, I feel sure that we are very fortunate for such prescriptions cannot be used in our state.

I was very much interested to know what Dr. Duke was going to say about the chronic use of adrenalin in allergic cases, because for several years I have been a firm believer in the use of adrenalin. We teach all patients with whom we deal how to use adrenalin, because I believe that a patient who is suffering from asthma, who knows how to use adrenalin, will be a much more practical individual. For example, if he is a business man traveling from our city to Chicago, he will realize that if he should have an attack of asthma on the pullman he has a means with him that will protect him from asthma. If he be at home, instead of wheezing, if asthma appears any hour of the night he realizes that he has a means of relieving his attacks, and consequently he will retire feeling very much better and without the worry that he would naturally have if he knew that he would have to suffer several hours or call a doctor for relief. Many patients as we all know will not call a doctor when they begin to wheeze, on account of the expense, or the inconvenience, and therefore will continue their wheezing and frequently produce an emphysema of the lungs, which in turn means cardiac failure.

I have often stopped and wondered whether we actually did damage in allowing a patient to continue the use of adrenalin over a long period of time. It has been my

experience, however, and the experience of others that I have talked to, that so far as we can see no damage is actually done. I talked to Dr. Walker about this matter last winter. I am very anxious to know how Dr. Pottenger feels about it. Personally, I feel that there can be little damage done from a drug that is a normal constituent of the blood stream. The effect of adrenalin is evanescent, which is another reason why I believe it is harmless. Surely it is not going to have the serious effect on the asthmatic patient that the long, strenuous effect of the asthmatic spasm would have.

In regard to morphine, I have seen very few allergic people who have developed a habit of using morphine. In our work with allergic cases we prescribe it very seldom. A narcotic inspector visited my office a few days ago and asked me to give an account as to why morphine prescriptions did not appear in the drug stores in Oklahoma City written by me. I told him I thought it was not any of his business. He looked at me very squarely and said, "In the state of Oklahoma I find prescription after prescription for morphine that is marked on the back, 'advanced asthmatic,' and I just wondered what you thought of the use of morphine for asthma."

Recently there was called to my attention by a nurse patient of mine in Amarillo the fact that two or three nights ago she had given some adrenalin in her thigh and it got to itching that night and hurting to some extent, which caused her to massage the area. The massaging of the area relieved a subsequent attack of asthma that had come on. About that time, a couple of weeks afterward, I noticed in the American Medical Journal a short note by Lilienthal concerning the use of adrenalin for the relief of bronchial attacks in postoperative cases of tuberculosis. Since that time we have tried it out on quite a few true asthmatics and find that in at least 75 to 80 per cent of them, if the attack of asthma comes within eight hours after giving adrenalin, that massaging the area will relieve the attack, which I believe is going to be of considerable help from the standpoint of the use of adrenalin. It means that adrenalin doesn't have to be given again and again. So many times a doctor will go into the country and give a dose of adrenalin to the patient, and in four or five hours from that time the patient is suffering again. Such an experience will cause him many times to give morphine instead of adrenalin. If by teaching that patient to massage the area relief can be had I think it will be considerable help in the use of adrenalin for the relief of asthma.

I would like to ask Dr. Pottenger to discuss one particular thing if he will, namely, why acute infections will relieve attacks of asthma. It is notoriously true that certain types of acute infections will relieve asthma. I have seen a good many cases in which an acute appendix, or scarlet fever, or typhoid, especially typhoid, relieved the patient from attacks of asthma for several months. I have one at present who has asthma with epilepsy and I once told the mother that if he could have any severe acute infection he would probably be free from asthma and also his epilepsy. He had an attack of scarlet fever and his epilepsy was gone for a year and is just now returning. Personally, I believe the toxin which stimulates the sympathetic nerve opposes the parasympathetic nerve, thereby giving relaxation.

Dr. Bernhard Steinberg, Toledo, Ohio.—The failure of adrenalin to relieve asthmatic attacks may be explained in some instances on anatomic grounds. The case I am to present illustrates this condition. The bronchioles, small and medium-sized bronchi are completely occluded by thick mucus which adheres to the walls of the tubes. If the result of the action of adrenalin is to dilate the bronchi, the adherent, thick mucus will prevent that action. The patient in this case was unable to raise any bronchial secretion.

Dr. F. M. Pottenger, Monrovia, Calif.—There are one or two things which I should like to say regarding the cases that Dr. Duke speaks of with low temperatures and high temperatures.

It was rather interesting that the whole picture of vagotonia or parasympathicotonia is a group in which anabolism is stronger than catabolism. That is characteristic of this group of individuals, and I think that is one of the reasons so many of them do have the lower temperature. They belong to the hypoglycemic type.

I was a little interested in what has been said about using insulin. I would hardly expect insulin to help the average case of asthma, particularly if it belongs to the hypoglycemic type which it usually does.

I think he points out a very interesting thing in this question of heat. When we are dealing with so many variables and so many things that interfere with our normal physiology, it is hard to pick out one variation which is always active.

With regard to the point brought out by the last gentleman, a few years ago I saw a little abstract of a paper by some one, I have lost the name and the reference. He found that in the secretions of the asthmatic there was a substance that produces a spasm of the smooth muscles, and this agrees with what we have just mentioned and also with what we should find. With a severe case of asthma during a period of paroxysms, I have given sodium iodide. Why? I want to get rid of the expectoration, so if you give sodium iodide, about fifteen or twenty c.c. intravenously and repeat every two or three days, you will find it will give tremendous relief, although it is opposed to the action of the calcium physiologically.

I raise the question of why acute infection produces relief from asthma. It cannot be answered entirely. I don't think we can point to any one thing, but you will find that any acute infection acts preeminently upon the sympathetic nerves. The whole peripheral picture of an infection expresses itself nervously on the sympathetic nervous system. There is more H than OH, acidity rather than alkalinity. A metabolic process is going on, with the temperature raised, and all the features that oppose the ordinary physiologic principles that are present in parasympatheticotonia. There is also during these periods a stimulation of the adrenals, with increased adrenalemia during infection. There is also increased stimulation of the thyroids during this period of reaction so that the whole physiologic mechanism that acts to oppose the parasympathetic mechanism is uppermost. I don't know the one thing to lay it to, but it seems to me that it is a complex affair in which many of the different systems are involved.

Dr. M. Murray Peshkin, New York City.—I have always felt that a discussion on the use and abuse of epinephrine hydrochloride in the treatment of asthma would be of timely interest. First of all it should be recalled that the physiologic action of adrenalin (1-1000) depends upon the quantity injected. Following the injection of a large dose of adrenalin (eight or more minims) the rate of the pulse is often increased thirty or more beats per minute, the systolic blood pressure is frequently raised to dangerous levels, the rate of respiration is increased, breathing at first becomes shallow and convulsive in character accompanied by tremor, pallor, cardiac palpitation, weakness and giddiness. Following the injection of a small dose of adrenalin (two to four minims) the picture is entirely reversed. The pulse and respiration rate are lowered, the depth of respiratory movement is increased and there is an absence of tremor, pallor, cardiac palpitation and weakness. The systolic blood pressure is frequently lowered ten or more millimeters of mercury. It is perfectly safe to administer two minims of adrenalin in an attack of asthma with a systolic blood pressure of 200 or more. If a patient is only partially relieved from an attack of asthma following the injection of a small dose of adrenalin, a second dose administered fifteen minutes later will invariably bring about relief, without causing symptoms that usually follow the injection of a single large dose of adrenalin. If this method of administering adrenalin were commonly employed I feel certain that the number of patients employing from one to two centimeters of adrenalin at one time and those with adrenalin tolerance would be considerably lessened.

It is extremely difficult to conceive of a human being escaping adrenalin tolerance after taking four ounces of the drug weekly, for several years. A patient with an acquired adrenalin tolerance usually gives a history of injecting the drug in progressively increasing doses. Such patients first came under my observation about nine years ago. Since then it has been my practice to break their tolerance for adrenalin by injecting eight minims each of adrenalin and extract of pituitrin (obstetric strength). This combination usually causes pain at the site of the injection for a period of several hours. The attack of asthma is not relieved as rapidly as when adrenalin is administered alone, but the relief

is more prolonged. This mixture is only employed for two or three weeks because after this period the patient may begin to show loss of weight. Now adrenalin alone can usually be effectively administered in small doses. If it is found necessary to give more than one dose of adrenalin at fifteen-minute intervals, then the possibility of the patient's acquiring adrenalin tolerance is very remote.

Concerning the after effects from the chronic use of adrenalin, I wish to state that more damage is inflicted upon the patient from the results of asthma rather than from the inteligent use of adrenalin. As a matter of fact the systolic blood pressure during an attack of asthma especially in patients past fifty years of age, frequently is raised twenty to sixty millimeters of mercury. In these patients adrenalin causes a marked reduction in blood pressure.

I cannot agree with the view that the restriction of adrenalin might be good practice in the patients taking the drug for a number of years. It is much more harmful to permit such patients to suffer through attacks of asthma with the additional danger of acquiring the incidental secondary organic changes in the lungs, bronchial tubes, heart, blood vessels and kidneys, I believe it is safer and more humane to give a patient as much relief from suffering as possible.

In a recent publication Dr. Howard Lillienthal of New York stated that asthmatic breathing can be relieved following massage of a site that has been injected with adrenalin several hours previously. His experience is limited to patients suffering with pulmonary tuberculosis. This procedure was carried out on a series of children with uncomplicated asthma with negative results.

Dr. I. S. Kahn, San Antonio, Texas.—I rather agree with Dr. Peshkin that these cases gradually in time develop more or less of a tolerance for adrenalin, and that is the reason they raise their doses. We usually get the history, as he said, of the attacks relieved by four, five, six or seven minims of adrenalin, maybe once a day, finally going up to three times a day, and many of these chronic adrenalin users, taking it for seven or eight years, have worked up to ten, twelve or fifteen minims, six or seven or even more times a day. As these cases of asthma are brought under proper allergy treatment, the doses of adrenalin are reduced.

With regard to Dr. Duke's suggestion of a heavy dose of aspirin and whisky, any of us would be glad to learn of any stunt that would help us out in cutting down adrenalin in severe asthma paroxysms. I have never tried a heavy dose of aspirin because I have always been afraid that a certain number of these cases might be sensitive to aspirin or other drugs, and have been afraid to try anything of the kind.

The thing that has given me most help in these cases has been small doses of ephedrin three times a day. The big trouble with these sick, chronic adrenalin using patients, is that they not only give negative skin tests as far as diagnosis is concerned, but such skin tests, even when negative, often appreciably increase the asthma. It has been my custom to try to get a diagnosis from the history and environmental study.

Regarding morphine, Dr. Duke told me a year or two ago that he never uses it, and Dr. Balyeat says he does not have to use morphine. If you go to a house and give fifteen or twenty minims of adrenalin for five or six doses, every twenty minutes or half hour, and your case shows no improvement, what can you do but give morphine? I do not see how we can get away from the use of morphine occasionally in a severe paroxysm of asthma. Of course, it is a bad thing to start. It is also true that a good many of these sick asthma patients will ask you not to give them morphine because they have an intolerance to it, it makes them sick, starts them vomiting, and they will beg you to hold off morphine just as long as you possibly can. I do not see, if you are going to handle very many sick asthmatic patients, how you are going to get away from the use of an occasional dose of morphine. In an acute attack of asthma, if adrenalin does not give relief after one or two repetitions, you are not going to get relief from adrenalin.

I had the pleasure of being in Dr. Duke's office a couple of years ago. He gave a beautiful demonstration of these physical agent cases of hay fever and asthma. He was able to produce hay fever of asthma by putting a patient under a lamp which gave out

heat or by rubbing the chest with ice. There isn't any question that he can bring on an attack of asthma and control it with heat and ice. I have always felt that he was dealing there, not with the original basis of asthma, but that his heat and cold sensitiveness was the same sort of secondary manifestation or secondary irritation that we could get in the cases which are brought on by paint, or varnish, or spraying the nose with oil of wintergreen or camphor. I have always felt his conditions were secondary.

Dr. Orville H. Brown, Phoenix, Ariz.—Just a word about adrenalin. I think in the main, patients have a tendency to use too large doses of adrenalin when a small dose would be just as effective as a large dose.

Burkhart found that a half minim was just as effective as four or five or more. I make it a point to keep the dosage below that which will give any signs of an overdose causing trembling, and so forth. I do not hesitate to repeat it as often as it is indicated in the smaller doses. I try to discourage going up over six or eight minims. Sometimes they seem to have an intolerance which makes it necessary to go above that, but as a rule, those who think they have to have those larger doses just think so, and the smaller doses will be just as effective. I don't know how to explain it.

I have used pituitrin with adrenalin. I have a preparation put out by some firm in England. I had to pay a heavy duty on it for a while which made it very expensive, but it certainly worked better than anything I ever used. It was said to be a combination of pituitary and ephedrin. In several severe cases which I had at that time it worked beautifully.

One thing that has not been mentioned here which I do wish to mention is the psychic state, particularly in these cases which have not had asthma long. The psychic state plays a tremendous part. The cough is partly psychic and partly due to irritation from the mucus and everything that is in the bronchi. The cough will help to aggravate the existing condition. For instance, you have a patient who is not in an attack, but is wheezing and will say his asthma is sticking around. If you have him put on several forceful exhalations, a half dozen, you will have him in an attack of asthma.

I have had some results by using sodium-iodide. Whether it is any better by vein than by mouth I do not know.

With regard to the use of aspirin, I have not hesitated to use it in those cases who know they can use it. I have had about six or eight cases which were sensitive to aspirin and would have a tremendous edema or asthma or some disturbance from the use of aspirin, but in other cases, one aspirin tablet a night, five grains, would cause the patient to get along very comfortably.

With regard to Dr. Duke's splendid work, I am a little bit like the last speaker. There are a great many sensitive individuals that do have some sort of a change when a cold draft blows upon them from the window or from a fan. I do not know whether that is due to something that is separate and distinct from the process which we may call sensitization or not. I follow Dr. Duke's work with a great deal of interest, and I am afraid I am overlooking some of these cases. I was in his office last year and he told me he knew I was, and I am certainly glad to have heard him this morning.

Dr. Harry L. Huber, Chicago, Ill.—I should like to have Dr. Duke answer one question. In these cases where he is using adrenalin, has he noticed a difference in its effect on patients with a high or low blood pressure? A large percentage of these asthmatics have very low blood pressures.

Dr. Alexander Sterling, Philadelphia, Pa.—I was under the impression that simultaneous administration of adrenalin and morphia is dangerous. I want to know whether or not it is so, and whether Dr. Duke had any serious results from the combined use of adrenalin and morphia.

The second point I should like to know is, in the administration of aspirin in asthmatics is it in the sensitive or in the nonsensitive type that he has found it of benefit. I have had occasions to use aspirin in patients who have the inflammatory or infectious type of asthma

whose asthmatic attacks alternate with mild or severe form of arthritis. Many of them do very well on aspirin in combination with some coal tar products.

Dr. William W. Duke, Kansas City, Mo.—I hope I have not made myself misunderstood in giving this paper on the continuous use of adrenalin. I do not wish to be understood as saying that continuous use of adrenalin in small doses is harmful. I think the use of enormous doses is harmful, and I do think it is harmful in patients using 300 drops a day. I have had three patients who used from three to four ounces a day. Two of these patients using it in enormous doses were emaciated to skin and bones and they were just as brown as if they had Addison's disease. That is harmful and I believe it is useless.

There isn't a patient under my care who takes over one c.c. of adrenalin a day. I am always able to get by with a small dose.

Concerning adrenalin intolerance, it is perfectly remarkable that you can get these people taking three or four ounces a day down in a relatively short time to where one c.c. will do them as much good as the large dose previously.

What are we going to do with morphine? Try more whisky and aspirin, because it is actually more effective than morphine. I can tell you frankly that if you give aspirin and a good big dose of whisky, sometimes an ounce or even two ounces (and I think whisky is more easily taken if sugar is added and you can get along with a smaller dose if sugar is added, and you can also warm it up a bit which causes quick absorption, and we want a quick anesthesia), it actually is more helpful in my cases than morphine. I have a worse time with asthmatics addicted to morphine. I practically do not use morphine in my cases, and have not for a number of years. I do not think it is necessary.

Now, about the blood pressure. Remember, the majority of blood pressures are down. Adrenalin lowers blood pressure in asthma. I do not know what the relationship is between adrenalin and the blood pressure. I possibly was misunderstood if I led anyone to believe that insulin, thyroid, peptone, or anything else takes the place of adrenalin.

With regard to stabilizing temperatures, I had one case which was subject to about fifteen or twenty short attacks of hives a day. If given a small dose of insulin in the morning, he would be free of his attack for four hours.

I had another case who was running a temperature and I believed she could be helped by changing her environment. She was living with a husband who was half insane and tormenting the dickens out of her. She was in a temperamental state of mind and everything would give her hives. When we got her away from home, however, her temperature did not sink to a low level.

With regard to pollen causing surface reactions, due to pollen sensitiveness, I have seen cases where they have changed and gone anywhere in the United States and still have asthma.

If you can make a person have a hive on exposure to light and nothing else in the world, that person is sensitive to light. If you can bring out a hive by a drop of cold water on the skin, that is a cold sensitive case, and if you can cure these patients by eventually increasing tolerance to light and by gradually increasing tolerance to cold, you have as much reason for saying that is a light sensitive case or a cold sensitive case as you have for saying a pollen case that is relieved by pollen or by getting away from pollen, is a pollen sensitive case. There are so many types of heat and cold sensitiveness it makes it difficult. You can always relieve by cold water a pure cold sensitive case. It is perfectly remarkable what you can do with them.

Pollen is not absorbed from the skin by application of light to the skin, especially in the winter time when there is not a speck of pollen in the air.

Concerning the administration of morphine and adrenalin, I have never used morphine in such a case. I will say morphine is dangerous to give under any conditions. If you are not taking up heat and cold sensitiveness, I believe you are passing up something. I believe it is due to some change in the heat regulating mechanism. For instance, a person may have a severe case of scarlet fever and after that become sensitive to heat and cold. A cause of sensitiveness in one person will relieve it in another, for one person

can be in bed with the body warm and breathe cold air and have an attack. If you place a towel so they will breathe moist, warm air, the asthma goes. The next case will be precisely the reverse. They will have their attack if they are in a warm room breathing warm air, and especially a little moist, and have their body cold. The cure here is to open the window and let the party remain there.

I want to mention one thing which I forgot to put in my paper. It is one of the experiments I have been carrying out. In a closed room in one of our offices, the total number of pollen grains that fell on the half inch slide in that room during the entire year was thirty. Pollen settles to the floor just as dust, and if you keep the windows closed and let the pollen fall to the floor, and have the room moist, you will have a room practically free of pollen. If the air is in motion it stays up. If the air is absolutely still, it stays down.

CLINICAL USE OF EPINEPHRIN IN ALLERGIC DISEASES

With Special Reference to a Method of Prolonging Its Effect and the Importance of Its Use in Cases of Asthma Complicated With Hypertension

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FOR the temporary relief of paroxysmal attacks of asthma no drug or combination of drugs has ever been added to the physician's armamentarium that equals epinephrin. For the purpose mentioned it is without question the drug par excellence. A newer drug, ephedrine, is a close second, but is a much weaker dilator of the bronchial muscle. The action of epinephrin when given hypodermically is usually rapid, and produces complete relaxation of the bronchial spasm, but its effect is evanescent. The drug would be of much greater value in the palliative treatment of asthma if its effect were more lasting. Therefore, any practical method of prolonging its action would surely be news welcomed by both the patient and the physician.

Several years ago surgeons used epinephrin in connection with novocaine almost routinely as a means of constricting the blood vessels in the field of operation, thereby holding the local anesthetic longer. Many of them, however, have discontinued the use of epinephrin for this purpose because of the secondary hemorrhage which frequently appeared from six to fourteen hours following the operation.

Luckhardt and Koppanyi[1] have shown experimentally that epinephrin hydrochloride can be given hypodermically to dogs with a rise in blood pressure from 15 to 180 mm. of mercury a few seconds following the injection. The blood pressure would return to normal in from ten to twenty minutes. Several hours later, when the area where epinephrin was given would be massaged, the blood pressure would again rise in a few seconds, but the extent of the rise would not be as great as the effect of the epinephrin given hypodermically.

Some weeks ago a nurse patient of mine, who suffers severely from asthma due to a Russian thistle sensitivity, called attention to the fact that after taking epinephrin and obtaining complete temporary relief from the asthmatic spasm, she could obtain a somewhat similar relief from a subsequent spasm, if it appeared within six to ten hours, by thoroughly massaging the area where the epinephrin was given. In a recent clinical note Lilienthal,[2] a surgeon, called attention to some observations he had made on postoperative cases of tuberculosis who suffered from a bronchial spasm, and he reported that they obtained relief from the use of epinephrin, and on massaging the area where epinephrin was given several hours later, at the time a subsequent spasm appeared, relief from the same was obtained.

For several years we have used epinephrin with some of the higher doses of pollen extracts in certain cases for the purpose of constricting the blood vessels, thereby allowing the extract to go into the system very slowly. In this way we found we could prevent systemic reactions that would manifest themselves in the form of asthma, hives, or hay fever, that otherwise would appear. This led us to believe that epinephrin remained in the local tissue over several hours. The experimental work of Luckhardt and Koppanyi is excellent evidence that epinephrin remains in the local tissue for several hours and that it can actually be liberated into the blood stream by massaging the area where epinephrin was given. The experience of the nurse, which was mentioned, is clinical evidence that epinephrin remains in the tissues and can be forced into the circulation by massaging the area where it was given. Lilienthal's experience in his surgical cases who suffered from a bronchial spasm or from true asthma associated with tuberculosis, is clinical evidence that a certain amount of epinephrin remains locally in the tissue and it can be liberated into the blood stream by massaging the area where it was given.

The experimental and the clinical evidence mentioned encouraged us to investigate the value of the massage method of sending into the circulation epinephrin for relief of subsequent attacks of asthma. It occurred to us that if massaging the area several hours later where epinephrin had been given to the patient for relaxation of the bronchial spasm, would throw into the circulation a sufficient amount of epinephrin to relieve the subsequent attack when it appeared, it would be of great practical value not only to men dealing with asthma as a specialty but also to the general practitioner. This somewhat preliminary report that we are making is based on a study of a series of twenty cases suffering from paroxysmal attacks of true asthma.

METHODS OF STUDY

Patients who came to the Clinic suffering from attacks of asthma were first worked out from the standpoint of their sensitivity, and if the attack occurred during the day they were asked to come to the office, at which time eight minims of epinephrin was administered subcutaneously, with notations concerning the relief obtained, and the effect of the epinephrin on their blood pressure. They were asked to return, on the appearance of another attack so that the area could be massaged by us and the clinical effect on symptoms and blood pressure made. Those whose asthmatic attacks appeared at night

were advised to take eight minims of epinephrin, and on the occurrence of another attack to massage the area, instead of giving epinephrin again, and report to us.

The following case reports give some of the details of the results.

CASE 1.—Mrs. R. L. F., aged thirty-five, had been suffering from moderate attacks of asthma each night for several weeks. She would frequently have to take a second dose of adrenalin. She was taught how to use her own adrenalin and was advised to follow the procedure as outlined above. Her attacks of asthma would occur about ten o'clock at night. She reported that adrenalin gave her almost instant relief, but the attack recurred about three o'clock in the morning, and on having the area massaged by her husband she obtained relief from the asthmatic spasm in three to five minutes. This procedure she repeated on a number of occasions, with relief each time. She found, however, on massaging the area twenty-four hours later, or in other words, ten o'clock the next night, she would obtain no appreciable relaxation from the bronchial spasm.

CASE 2.—Miss M. D., a nurse, aged forty, who had suffered from moderately severe attacks of asthma and had been using adrenalin for several months. She had learned several months ago that massaging the area where the adrenalin was given, at the time the subsequent attack would appear, would give her relief, if the second attack occurred the same night.

CASE 3.—Mrs. R. K., aged thirty-seven, has suffered severely from asthma due to Russian thistle sensitivity for the past three years. Her attacks would usually occur early in the night, and by the use of adrenalin she obtained relief. In the early hours of the morning, by following the instructions given her concerning the massage method, she could obtain relief in from three to five minutes.

This patient was suffering from a severe attack of asthma while in the office, for which eight minims of adrenalin was given. Before adrenalin was given her blood pressure was systolic 110, diastolic 80. Three minutes after the injection of adrenalin the blood pressure was 124 systolic, diastolic 80 and she complained of nervousness, with a peculiar feeling in the abdomen, of which a great many patients complain following the use of adrenalin. Four hours later, while she was not suffering from asthma, the area where the adrenalin was given was massaged, to find the blood pressure to change from 110/80 to 118/80. At this time she also observed the general nervous feeling and peculiar feeling in the abdomen, as she noticed at the time the adrenalin was given hypodermically.

CASE 4.—Mr. V. C. M., aged thirty-eight, a patient we have observed for several months, who recently has had to use adrenalin every night. He was given eight minims of adrenalin while suffering from an attack of asthma, by one of the members of the Clinic, on three occasions. Each time it was observed that his blood pressure would elevate from ten to twenty points above the normal, from the use of the adrenalin. On massaging the area from four to eight hours later the blood pressure would elevate several points, but not as much as at the time the adrenalin was given hypodermically. However, at the time of massaging he would always have the nervous symptoms which he observed when adrenalin was first given.

His arm where adrenalin was given was massaged the second day, that is, twenty four hours later, on two occasions, without any symptoms, or without relief from the spasm for which he had come in complaining.

CASE 5.—Mrs. M. R., aged fifty-nine, an asthmatic patient of long standing who has been perfectly controlled so far as her asthma was concerned. To this patient adrenalin was given. Blood pressure readings were made and nervous symptoms observed. Her blood pressure changed from 140/80 to 154/80 following the use of adrenalin hypodermically. Eight hours later massaging the area where adrenalin was given changed the blood pressure systolic from 140 to 148 and produced marked nervous symptoms, which she had also encountered at the time the adrenalin was first given.

CASE 6.—R. B., aged four, a doctor's son, whom I saw at ten o'clock one night, when he was given six minims of adrenalin, and I was immediately told by the mother that his attack would recur as they had been doing so every night, and therefore the boy would have to have another hypodermic of adrenalin. She was instructed to massage the arm thoroughly where the adrenalin was given and was told that it might relieve his attack, thereby not making it necessary to give the second hypodermic. The massage method was tried at five o'clock the next morning by the boy's father, a physician, with complete relief from the attack. The subsequent attack was very severe, awakening the boy from a sound sleep.

Other cases studied have given us somewhat similar results. In fact, but few cases on whom we tried the massage method or who used the massage method themselves within the first eight hours, failed to find partial or total relief from the asthmatic spasm.

From our findings it appears that massaging the area where epinephrin was given, from four to eight hours later, at the time the subsequent asthmatic attacks occur, will relieve the spasm in most cases. Those doing general practice who frequently see patients suffering from an acute severe attack of asthma, for example at ten to twelve o'clock at night, will usually find, if the attack is very severe, that it will recur from four to eight hours later. If such patients could obtain relief from the subsequent attacks by massaging the area thoroughly, it appears to the writer that it would eliminate the greatest objection to the use of epinephrin in the palliative treatment of asthma, namely, its evanescent action.

The series of cases we have studied up to the present, which is less than two dozen, is of course not sufficient to justify our drawing definite conclusions as to the value of prolonging the effect of epinephrin and thereby increasing materially its value in the treatment of asthma, but the results are so interesting and so full of possibilities that we feel justified in making this somewhat preliminary report.

USE OF EPINEPHRIN IN CASES OF ASTHMA COMPLICATED WITH HYPERTENSION

Since one action of epinephrin is that of elevating the blood pressure it is natural for one to feel that in case of asthma associated with hypertension it would be contraindicated. During the last eight years it has fallen to my lot to care for a number of cases of true asthma complicated with hypertension, also many cases of cardiac and cardiorenal asthma. For a long time we tried to stay away from epinephrin and use other means of controlling the asthmatic spasm in the cases complicated with hypertension. However, observing the wonderful relaxing effect of epinephrin upon the bronchial muscle in true asthma, we began to use routinely in very small doses this same drug in cases of true asthma complicated with hypertension and in the cardiorenal type of asthma, and we wish to report three cases which typify the results.

CASE 1.—Dr. A. M., aged sixty-two, came to the Clinic suffering from seasonal hay fever and very severe paroxysmal attacks of asthma, of three months' duration. On examining him he was found to be extremely sensitive to pollen and also to animal dander. His blood pressure was 240 systolic and 100 diastolic. The urine examination was negative. The question naturally arose as to whether this man with a blood pressure of 240 should have adrenalin for the relief of his asthma. He was given five minims of adrenalin, and at the same time blood pressure observations were made.

During the twenty minutes following the injection of the adrenalin the blood pressure did not change. He obtained considerable relief from the asthmatic spasm. Two hours later eight minims of adrenalin was given, with complete relief from the asthmatic spasm, with an elevation of systolic pressure only four points. From that time on he was advised to use adrenalin himself as often as necessary for the relief of attacks, which he did, and in three days his blood pressure readings were 180 systolic, 100 diastolic.

CASE 2.—Mrs. A. W. F., aged fifty-eight, suffered with phthisic as a small child. During the last five years she has suffered from hypertension and moderately severe attacks of asthma. She was sensitive to animal epithelial only. Her physical examination revealed a blood pressure of 220/120. The liver edge could not be felt. The urine examination was normal. Here again the question arose as to whether adrenalin should be given for the relief of the asthmatic symptoms.

She was tested out with small doses of adrenalin hydrochloride and the blood pressure carefully watched, without appreciable elevation. Larger doses were then used in sufficient quantity to relieve the attacks, with elevation of the systolic pressure only from three to five points. By keeping down the attacks with the use of adrenalin her blood pressure finally stayed at 190/120. This patient of course was advised to rest a great deal and she was put on a low protein diet on general principles. During the last few months she has done exceptionally well for one with the complications she has had. She has to continue to use adrenalin from time to time for the relief of her asthmatic symptoms.

CASE 3.—Mrs. W. L. S., aged sixty-one, came with a history of hay fever for twenty years and asthma for the past five years. Physical examination showed a blood pressure of 160/110 when he was not wheezing, but during an attack he would have a blood pressure of 190/110. Here again adrenalin was used with relief of his attacks, without dangerously elevating his blood pressure.

DISCUSSION

In cases of hypertension it is routine with most doctors to advise them not to get angry, not to walk against the wind, not to climb stairs, not to lift heavy loads, etc. In other words, to do nothing that would have a tendency to elevate the blood pressure. We can conceive of nothing that would throw a greater load on the heart and would have a greater tendency to elevate blood pressure than severe paroxysmal attacks of asthma.

Our clinical observations on these cases have shown us that moderate size doses of epinephrin in cases of true asthma complicated with hypertension or in cardiorenal cases, will raise the systolic blood pressure but little. Therefore, it seems to us that in cases of true asthma complicated with hypertension, or in cases of hypertension with a failing heart, or cardiorenal cases suffering from labored breathing, paroxysmal in type, that some efficient means should be used to relieve the spasm. Knowing that there is no preparation that equals epinephrin for this purpose makes us feel that it should be tried out routinely in small doses, and if it does not elevate the blood pressure appreciably it should be used for the relief of the asthmatic spasm. Assuming, for the sake of argument, that it does in some cases elevate the blood pressure, for example, even ten or twenty points, how much better it would be for epinephrin to elevate the systolic blood pressure which stands at 240, ten points for twenty minutes, but at the same time relieve them of their asthmatic spasm so that the pressure on its own accord would lower 50, 60 or even 80 points, than it would be to allow the systolic blood pressure to stand at the height mentioned over a period of several hours while they are wheezing.

EPINEPHRIN IN HAY FEVER

Preparations of epinephrin, either aqueous or otherwise, in my opinion, should never, or seldom ever, be used on the mucous membrane of the nose of hay fever patients for the relief of congestion, since there is a secondary vasomotor dilatation which has a tendency to make symptoms more severe than they were before its use. It is fairly well recognized by the rhinologist that the continued use of epinephrin on the membrane of the nose does harm. For the temporary relief of eye symptoms in hay fever it should probably never be used.

During the efficient treatment of hay fever with potent pollen extracts it is not uncommon to encounter a systemic reaction, manifesting itself in the form of hives, asthma, or hay fever, as one nears or reaches the tolerance dose, and for the relief of such symptoms there is no drug that will give better results than epinephrin given hypodermically in from ten to twelve minim doses. The untoward symptoms may reappear in from two to four hours, or even eight hours, and if they do, the area where the epinephrin was given may be massaged for relief, or a second dose of epinephrin can be given.

In pollen therapy epinephrin is also of considerable value in blocking the blood supply where some of the high doses of the extract are given, so as to allow it to enter the system more slowly, thereby preventing a systemic reaction. For example, certain patients may take 0.25 c.c. of the 1:500 dilution of an extract of grass or ragweed, or any other pollen, and from it encounter a systemic reaction. On dropping back a notch or two in schedule and building again they are not able to pass the same size dose without a similar experience. However, by drawing into the syringe, after the 0.25 c.c. of the pollen extract is in the syringe, three to four minims of epinephrin, and injecting that first into the subcutaneous tissue, and waiting a few seconds and then injecting the pollen extract, the systemic reaction will not be encountered, since epinephrin constricts the blood supply just as it does when the surgeon uses it along with novocaine, and thereby allows the material to enter the circulation over a period of several hours instead of most of it going in within a few minutes' time. On the next regular treatment day a dose of pollen extract still higher may be given, and a higher and still higher dose, etc., allowing one to carry the pollen extracts several doses higher in schedule, even up to a point where the patient will be fully protected from hay fever or asthma, who otherwise would not obtain relief from his hay fever or asthma symptoms on account of his tolerance dose being too low.

In at least 40 per cent of our hay fever cases we encounter systemic reactions before the patient is carried as high as we know they must be for protection. By means of epinephrin used as we have just outlined they can be carried sufficiently high to relieve them from their hay fever or asthmatic symptoms. It must not be forgotten, however, that when epinephrin is once used for the purpose of carrying the patient higher with pollen extracts, it must always be used.

EPINEPHRIN IN URTICARIA

For the temporary relief of acute attacks of urticaria due to food poisoning, serum sickness, bites from insects, etc., epinephrin in from six to twelve minim doses will usually give relief. However, it may have to be repeated, and here again we have found that massaging the area where epinephrin was given, in the few cases we have tried, will give relief from the subsequent symptoms that appear. If in cases of stings from insects or idiosynerasies to foods or drugs, there are symptoms of severe abdominal pain, with swelling of the tongue or soft palate, epinephrin should be given in from ten to fifteen minim doses hypodermically, and the throat should be swabbed with a 1:1,000 dilution. Several cases of death due to asphyxia have been reported from edema of the soft palate following stings from insects.

ASTHMATIC PATIENTS SHOULD BE TAUGHT HOW TO GIVE THEMSELVES EPINEPHRIN

It has been my custom[3] during the last eight years to teach the asthmatic patients who come to our Clinic how to give epinephrin to themselves. Some doctors raise the question as to whether this should be done, saying that patients might form the habit of using opiates, and, too, that the danger of infection is great. During our eight years of care of allergic patients more than fifteen hundred cases of asthma have been studied, and at least one-third of these have been taught to give epinephrin to themselves. So far as we know not a single one of them today is a drug addict, and no case of infection has been reported. It is our opinion that the patient is going to use some drug for the relief of his symptoms, and therefore he should be taught how to use the best drug available.

For the relief of the asthmatic attack the best results are obtained by giving the epinephrin at the onset, and not after the patient has wheezed for four or five hours. If they do not know how to give themselves epinephrin, they usually wait awhile to see if the attack will not subside, and then a doctor is called, at which time the spasm is extremely severe. Frequently the doctor does not arrive for from two to six hours, which means that the patient has suffered several hours from his asthma, thereby not only depleting his system but producing emphysema. For the relief of such symptoms after the doctor arrives it will require from ten to twelve minims of epinephrin. The same relief in all probability could have been obtained with from four to five minims of the drug if given early. Many patients of course will suffer throughout the night instead of calling the doctor on account of financial circumstances.

Doctors so frequently tell patients that epinephrin will harden their arteries if taken over a long period of time and that it is a drug that is habit-forming. Of course any drug that has to be taken frequently is probably somewhat harmful, some of them much more harmful than others, of course, but since epinephrin is a normal constituent of the blood stream it will naturally have less deleterious effect on the patients than most drugs. Assuming that it might be somewhat harmful, how much less damage it would do than

the severe attacks of asthma that would continue for hours at a time. The end-results of unprotected asthma are emphysema, bronchiectasis and heart failure.

In teaching patients to give themselves epinephrin it has been our custom to have them always use alcohol for sterilizing the syringe and needle, as we feel that the danger of infection is much less than if the needle and syringe are boiled, as their fingers will have a less tendency to come in contact with the needle by this method of sterilization.

Asthmatic patients who have suffered severely over a period of time dread very much the thoughts of attacks. For this reason we teach our patients never to be without epinephrin. Even if they have been free several months they should carry the epinephrin and syringe for giving, and material for sterilization, when they go on their vacations or on business trips, so that they can always feel that they have at their command a product for the relief of the paroxysmal attack of asthma that might appear. Such an arrangement not only makes them feel more confident of themselves from the standpoint of doing the ordinary things of life that other people do, and thereby making men in business more practical, but they enjoy life so much more since they do not have to live in the dread of a severe attack of asthma without means of protection.

In about 85 per cent of the cases we studied, from 60 to 100 per cent relief from symptoms can be given, but such relief is not obtained at once. It usually requires, for treatment of many cases of asthma, several months, and during this time it is of great importance that every attack of asthma possible be kept down by some simple means, and there is no drug of greater importance, and less harmful for this purpose, than is epinephrin.

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THE INFLUENCE OF ANIONS AND KATIONS ON THE VIABILITY OF BACILLUS COLI*

By C. H. Boissevain, M.D., and Eric Webb, M.D., Colorado Springs, Colo.

Ficker[1] first showed the bactericidal action of distilled water and physiologic salt solution. The viability of the cholera vibrio disappears after two or three days, if not more than 60,000 organisms are present in each cubic centimeter. In the presence of greater numbers a large percentage of them die in the first hours, but the survivors multiply at their expense. The addition of 1 per cent nutrient broth to the 0.7 per cent NaCl solution also neutralizes the bactericidal effect. Legroux and Eliava[2] found that the number of vibrio cholera, staphylococci, and bacillus anthracis remains constant when suspended in distilled water to which 0.6 per cent of blood corpuscle extract had been added; the organisms die more or less rapidly if less extract is used. Panisset, Verge and Carneiro[3] found that 0.8 per cent NaCl solution was more toxic than distilled water for staphylococci, typhoid, coli, Friedlaender and anthrax bacilli. Loeb[4] showed that the toxic effect of NaCl on living cells could be neutralized by the addition of appropriate concentrations of potassium or calcium salts. This suggested the work of Sherman and Holm[5, 6, 7] and of Winslow and Falk.[8] They found that the toxic effects of NaCl may be neutralized by the addition of $CaCl_2$. The optimal concentration, according to Winslow and Falk, is four parts NaCl to one part $CaCl_2$, with a total concentration of 0.725 M. The effect is most noticeable in alkaline solutions. Hotchkiss[9] found that all chlorides prevent the growth of B. coli, if added in sufficient concentration to 1 per cent peptone water; the chlorides of the alkalis are least toxic, followed by the chlorides of the alkaline earths, while those of the heavy metals are most toxic. Shaughnessy and Criswell[10] found that the B. coli of their strain increased in number when suspended in distilled water; their distilled water was, however, buffered by the addition of Northrop and DeKruif's buffer solutions, which obviously introduces an error.

Most of the work on the effects of electrolytes on the viability of bacteria has been concerned with differentiating between the action of the kations, and with efforts to find "balanced" solutions, in which the number of bacteria remains constant. Sherman and Holm[5] find that Cl, I, NO_3, SO_4, PO_4, accelerate growth of B. coli in peptone water, all other anions retard it. They found little difference between Na, K, and NH_4; Mg was more toxic and Ca most. Little other work has been done in regard to the anions; Falk[11] in his comprehensive review of the action of ions in physiology does not even refer to them. This lack of attention has been caused partially by the in-

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Received for publication, January 17, 1928.

teresting discoveries of the physiologists about the antagonism between Na, K, and Ca in the contraction of smooth muscles, and partially by the attention that has been given in later years to the phenomena connected with Donnan's membrane equilibria. Northrop and DeKruif[12] showed that the isoelectric point of the typhoid bacillus is situated at a hydrogen-ion concentration of P_H 3.0. It follows from Donnan's equation, that only kations can influence the osmotic and electric properties of bacteria suspended in solutions more alkaline than P_H 3.0. It does not follow, however, that only the kations can be of importance for the viability of the bacteria. In applying Donnan's equation to bacteria, it is tacitly assumed that these are equally permeable for all simple ions. The possibility exists that this is not the case, and that the bacterial membrane is only, or at least mainly, permeable for anions, as is e.g., the case for erythrocytes. It is the purpose of this paper to show that the effect of the anions on the viability of B. coli is far greater than that of the kations.

We have limited our studies to the anions Cl^-, $SO_4^=$, NO_3^-, and $HPO_4^=$ and to the kations K^+, Na^+, Ca^{++}, Mg^{++}, as they seem most important from a physiologic point of view. Other factors included in the present study were the influence of the osmotic pressure and of the P_H in the hope of determining which part of the salt effect is due only to the chemical nature of anions, and which part is due to other factors.

METHODS

A strain of Bacillus coli communis was chosen for this work, because of its small tendency to spontaneous agglutination. In using staphylococci as some workers did, a complication was introduced by the possibility of a disintegration of the clumps of cocci, which would simulate an increase, when colonies were counted by the plate method. A twenty-four-hour broth culture was used, which was filtered through Whatman filter paper No. 5 and diluted 125,000 times; 0.1 c.c. of this dilution was added to 8 c.c. of nutrient agar at 45° C., plates poured and the colonies counted after twenty-four hours in the incubator at 37° C. This whole process of preparing the dilutions and pouring the plates did not take more than five minutes.

This method was preferred to the use of a washed and filtered suspension of bacilli grown on solid medium because the washing and centrifuging takes considerable time; preliminary experiments showed that the death rate of the coli bacilli in salt solutions is highest in the first hour, as shown in Chart I. In some experiments as many as 60 per cent died in the first hour, while a few of the more resistant bacilli were still alive after twenty-four hours. The difference between the different salt solutions must be most evident immediately after mixing the bacteria with the solutions. This difference in resistance that is seen between the single bacilli, can sometimes be observed between broth tubes inoculated with the same strain of bacteria. These changes in the percentage of resistant individuals in a broth culture affect uniformly the resistance against all salt solutions and do not affect the results. The amount of culture medium carried over in the 1/125,000 dilution is much smaller than

the 0.6 per cent necessary for the growth of bacteria in NaCl solution, as we could verify in experiments performed for that purpose.

Bacilli remain alive longer in the same salt solution when kept in the ice box at 4° C. than in the incubator at 37° C. All our experiments were performed at room temperature (20° C.).

The salt suspensions with bacteria were kept in the dark as much as possible, because the diffuse daylight at the altitude of Colorado Springs (6000 feet) has a decided bactericidal action.

Another point of some importance is the use of pipettes of uniform diameter. A considerable number of bacteria is always absorbed on the walls of the pipette, and this effect will vary with its diameter. When several pipettes are used for succeeding dilutions, the error increases in geometric progression and may become large.

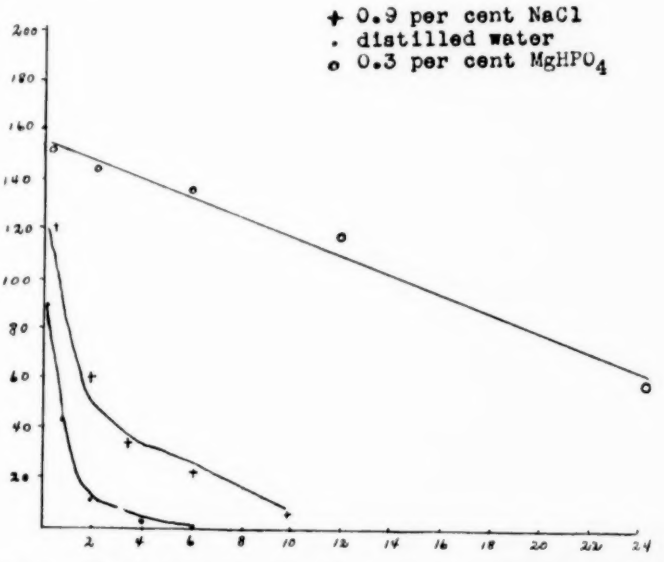

Chart I.—Number of colonies grown from 0.1 c.c. of 1/125,000 dilution in distilled water, 0.9 per cent NaCl and 0.3 per cent $MgHPO_4$. The abscissa indicates the number of hours elapsed since making the dilutions, and the ordinate the number of colonies.

It seemed possible that the harmful effect of salt solutions was simply caused by the sudden transition from one medium to another. A bacillus that had been accustomed to a synthetic medium of a definite composition would in this case react differently to this salt concentration from a bacillus grown in broth. To determine this influence, we grew a colon bacillus through a series of seven transplants in a medium of the following composition:

Asparagin	0.1 per cent
Glucose	0.1 per cent
$MgHPO_4$	0.1 per cent
KCl	0.1 per cent

Dilutions of these bacilli and of bacilli grown in ordinary broth were made in a medium of the following composition:

$MgHPO_4$	0.1 per cent
KCl	0.1 per cent

and the death rates in the two cases compared. The results are given in Table I. Since there is no appreciable difference between the death rate of the bacilli, we conclude that no error is introduced by using bacilli grown in nutrient broth.

TABLE I

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF DILUTION, WHEN THE BACILLI HAD BEEN GROWN IN DIFFERENT MEDIA

TIME ELAPSED SINCE MAKING DILUTIONS	BACILLI GROWN IN SYNTHETIC MEDIUM (DILUTION 1/12,500)	BACILLI GROWN IN BROTH (DILUTION 1/125,000)
0 hours	245	612
3½ hours	238	587
7 hours	150	522
24 hours	28	56

EXPERIMENTAL

Effect of osmotic pressure.

A. Nonelectrolytes.—The effect of distilled water on the coli bacilli was compared with that of different concentrations of urea and glucose. The results are given in Table II.

The maximum number of survivors is in the urea solution of one-fourth molar concentration; both higher and lower concentrations are less favorable.

The results with glucose solutions are somewhat different: less than one-fourth molar concentrations show the highest death rate, but no appreciable difference could be shown between one-fourth molar and higher concentrations. The most probable explanation seems that the glucose can penetrate into the bacilli and so equalize the difference in osmotic pressure; only the effect of the lower osmotic pressure can be demonstrated under these circumstances. It is interesting to note that neither of these solutions acts as a nutrient medium.

TABLE II

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN DIFFERENT UREA CONCENTRATIONS

TIME ELAPSED SINCE MAKING DILUTION	CONCENTRATION OF UREA				
	1/16 M	1/8 M	1/4 M	1/2 M	1/1 M
0 hours	211	207	182	204	185
2 hours	14	109	129	87	52
4 hours	2	8	19	5	1

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN DIFFERENT GLUCOSE CONCENTRATIONS

TIME ELAPSED SINCE MAKING DILUTION	CONCENTRATION OF GLUCOSE						
	DIST. WATER	1/50 M	L/16 M	1/8 M	1/4 M	1/2 M	1/1 M
0 hours	91	91	68	97	82	91	74
4 hours	1	1	1	7	15	27	14
24 hours	0	0	0	0	0	0	0

B. Electrolytes.—The effects of different concentrations of NaCl, KCl, $CaCl_2$, K_2SO_4, $KHPO_4$, $NaHPO_4$, were compared; in the case of the phos-

TABLE III

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN SOLUTIONS CONTAINING DIFFERENT CONCENTRATIONS OF THE FOLLOWING SALTS: NaCl, KCl, $CaCl_2$, K_2SO_4, MIXTURE OF Na_2HPO_4 AND NaH_2PO_4, MIXTURE OF K_2HPO_4 AND KH_2PO_4 (P_H OF ALL SOLUTIONS: 7.0)

TIME ELAPSED SINCE MAKING DILUTIONS	CONCENTRATION OF NaCl				
	DIST. WATER	1/50 M	1/16 M	1/8 M	1/4 M
0 hours	64	107	90	59	65
8 hours	0	1	3	17	9

TIME ELAPSED SINCE MAKING DILUTIONS	CONCENTRATION OF KCl					
	DIST. WATER	1/50 M	1/16 M	1/8 M	1/4 M	1/2 M
0 hours	103	92	94	92	120	110
7 hours	2	1	3	51	34	7

TIME ELAPSED SINCE MAKING DILUTIONS	CONCENTRATION OF $CaCl_2$					
	DIST. WATER	1/50 M	1/16 M	1/8 M	1/4 M	1/2 M
0 hours	135	135	146	191	192	129
5 hours	0	0	26	9	1	0

TIME ELAPSED SINCE MAKING DILUTIONS	CONCENTRATION OF K_2SO_4					
	DIST. WATER	1/50 M	1/16 M	1/8 M	1/4 M	1/2 M
0 hours	160	285	273	202	192	215
5 hours	0	2	2	15	6	9

TIME ELAPSED SINCE MAKING DILUTIONS	CONCENTRATION OF Na_2HPO_4 PLUS NaH_2PO_4					
	DIST. WATER	1/50 M	1/16 M	1/8 M	1/4 M	1/2 M
0 hours	87	132	208	122	124	104
8 hours	0	104	186	108	62	68
24 hours	1	69	541	431	299	90

TIME ELAPSED SINCE MAKING DILUTIONS	CONCENTRATION OF K_2HPO_4 PLUS KH_2PO_4					
	DIST. WATER	1/50 M	1/16 M	1/8 M	1/4 M	1/2 M
0 hours	113	167	146	162	139	128
7 hours	0	82	181	228	207	97
24 hours	0	17	254	±3000	±1500	59

phates a mixture of primary and secondary phosphates of P_H 7 was used. The results are given in Table III.

The optimum concentration for most of these salts is at 1/8 M concentration. The only exception is $CaCl_2$, which has its optimum at 1/16 M. Theoretically we must expect an optimum at 1/12 M for all salts that dissociate in 3 ions. Only the calcium chloride gives evidence of a lower optimum than 1/8 M. The results are, however, complicated by the fact that the anions are responsible for the toxic action of the salts, as we shall show later. The toxic anion is approximately 2 times more concentrated in a calcium chloride solution than in an equimolecular sulphate solution, and its harmful effects must appear at a lower concentration.

EFFECT OF IONS IN EQUIOSMOTIC CONCENTRATION

A. Kations.—The effects of 1/8 M solutions of NaCl and KCl were compared to 1/12 M solutions of $CaCl_2$ and $MgCl_2$; the results are given in Table IV.

Very little difference is found between the action of NaCl and KCl on one side and that of $CaCl_2$ and $MgCl_2$ on the other. The chlorides of the bivalent

salts are, however, more toxic for the colon bacillus than those of with univalent kations, the concentration of Cl^- ions being higher in equiosmotic solutions.

B. Anions.—The effects of solutions of NaI, NaCl, Na_2SO_4, $NaNO_3$, and $NaHPO_4$ were compared; the results are given in Table V. The toxic effects of the anions depend apparently upon the chemical nature of the ion and no evidence is found of the valency effect that we found in the case of the kations. The phosphates are most favorable and even cause an increase in the number of bacilli. After the phosphates follow the ions NO_3^-, Cl^-, SO_4^-, I^-, in the order given.

TABLE IV

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTIONS IN CHLORIDES WITH DIFFERENT KATIONS

TIME ELAPSED SINCE MAKING DILUTIONS	NaCl 1/8 M	KCl 1/8 M	$CaCl_2$ 1/12 M	$MgCl_2$ 1/12 M
0 hours	90	79	74	113
2 hours	71	59	3	13

INFLUENCE OF P_H

Sodium phosphate solutions of different P_H were compared. The results are given in Table VI.

The influence of the P_H of phosphate solutions is evidently of small importance as long as it remains above 5 and below 8.

ADDITIVE EFFECT OF IONS

In the first place physiologic salt solution was compared with Ringer's solution and with salt solutions to which only K or Ca has been added in the same concentration as in Ringer's solution. The results are given in Table VII.

There appears to be very little difference in the action of these solutions on the viability of the coli bacillus.

We next compared two solutions containing respectively 0.58 M NaCl and 0.145 M $CaCl_2$, with a solution containing both. The results are given in Table VIII.

Winslow and Falk state that the solution containing both NaCl and $CaCl_2$ is less toxic than the solution containing only one of those salts. Our experiments give no evidence of "balancing" the toxic action of NaCl by that of $CaCl_2$; the effects were purely additive.

Similar results were obtained by mixing equal parts of 1/8 M NaCl with 1/8 M $NaNO_3$ solution. The results are given in Table IX.

TABLE V

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTIONS IN 1/8 M SODIUM SALTS WITH DIFFERENT ANIONS (IN THE CASE OF SODIUM PHOSPHATE A MIXTURE OF PRIMARY AND SECONDARY PHOSPHATES OF P_H 7.0 WAS USED)

TIME ELAPSED SINCE MAKING DILUTIONS	NaCl	NaI	$NaNO_3$	Na_2SO_4	SOD. PHOS.
0 hours	123	60	114	78	112
2 hours	82	0	105	52	116
5 hours	31	0	100	1	108

TABLE VI

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN 1/8 M SODIUM PHOSPHATE MIXTURES OF DIFFERENT P_H

TIME ELAPSED SINCE MAKING DILUTIONS	P_H OF THE SOLUTIONS				
	5	6	7	8	9
0 hours	76	108	83	106	103
4 hours	92	97	100	77	1
8 hours	102	136	194	135	0
24 hours	159	1200	5000	82	0

TABLE VII

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN 0.8 PER CENT NaCl SOLUTION AND IN RINGER'S SOLUTION

TIME ELAPSED SINCE MAKING DILUTIONS	0.8% NaCl	0.8 % NaCl 0.02% KCl	0.8 % NaCl 0.02% KCl 0.02% $CaCl_2$	0.8 % NaCl 0.2% $CaCl_2$	RINGER'S SOLUTION
0 hours	170	157	162	191	187
4 hours	68	73	27	65	56

TABLE VIII

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN 0.58 M NaCl, 0.145 M $CaCl_2$, AND 0.58 M NaCl PLUS 0.145 M $CaCl_2$

TIME ELAPSED SINCE MAKING DILUTIONS	0.58 M NaCl	0.145 M $NaCl_2$	0.58 M NaCl PLUS 0.145 M $CaCl_2$
0 hours	107	99	97
4 hours	81	44	12
8 hours	38	2	1
12 hours	25	0	0

This experiment is not quite comparable to that of Table VIII. In that case we had, following the example of Winslow and Falk, added the $CaCl_2$ to the solution containing the NaCl, thus changing the osmotic pressure. In the experiment of Table IX the osmotic pressure remained constant, although half of the Cl^- ions had been replaced by NO_3^- ions. The mixture of chloride and nitrate was a little more toxic than the nitrate solution and a little less than the chloride solution.

If a sodium chloride solution is mixed with an equal quantity of sodium phosphate (P_H 7), the toxic effect of the sodium chloride is completely compensated, as is shown in Table X.

The bacteria are even able to increase their number in the solution containing both phosphate and chloride. The increase was somewhat less in the solution containing both anions than in that containing only phosphates. The total increase may be compared with that shown in a 1/16 M sodium phosphate solution. Similar results were obtained when potassium phosphate was used or when sodium sulphate took the place of the sodium chloride.

INCREASE OF NUMBER OF BACILLI IN PHOSPHATE SOLUTIONS

The number of bacilli increased in several instances when they were suspended in phosphate solutions in the apparent absence of all nutrient constituents. We first thought that this might be due to an increase at the expense of dead bacilli and made serial transplants into other phosphate solutions; the increase could still be observed after the seventh transplant. We

now repeated the experiment in quartz tubes stoppered with glass wool. The number of bacteria remained now constant, and decreased proportional to

TABLE IX

NUMBER OF COLONIES GROWN FROM 0.1 C.C. OF 1/125,000 DILUTION IN 1/8 M NaCl, 1/8 M $NaNO_3$, AND 1/8 M NaCl PLUS 1/8 M $NaNO_3$

TIME ELAPSED SINCE MAKING DILUTIONS	1/8 M NaCl	1/8 M $NaNO_3$	1/8 M NaCl PLUS 1/8 M $NaNO_3$
0 hours	97	61	75
2 hours	4	48	15
6 hours	0	7	1

TABLE X

NUMBER OF COLONIES GROWN FROM 0.1 C.C OF 1/125,000 DILUTION IN 1/8 M NaCl SOLUTION, IN 1/8 M PHOSPHATE SOLUTION (MIXTURE CONTAINING PRIMARY AND SECONDARY SODIUM PHOSPHATE OF P_H 7.0), AND IN A 1/8 M SOLUTION CONTAINING EQUAL PARTS OF 1/8 M NaCl AND 1/8 M PHOSPHATE SOLUTION

TIME ELAPSED SINCE MAKING SOLUTION	NaCl 1/8 M	SOD. PHOS. 1/8 M.	NaCl 1/8 M PLUS SOD. PHOS.
0 hours	76	55	55
6 hours	9	70	66
12 hours	0	90	73

the dilution in serial transplants. The colon bacillus is apparently able to satisfy its needs of nitrogen from the air, while bits of charred cotton fallen into the solution from the usual cotton stoppers are sufficient source of carbohydrates. This is especially remarkable when we remember that no increase in the number of bacteria took place in the urea or glucose solution. The only mineral constituent that the colon bacillus needs for reproduction is the phosphate ion. If sufficient phosphate is present, minimal impurities are sufficient for the life of the colon bacillus. The nature of the kation combined with the phosphate ion is without importance. We do not want to suggest that this is a general property of all bacteria; one of us[13] has shown that the tubercle bacillus needs the presence of either potassium or rubidium for growth. Further study will have to show whether all bacteria need only the presence of phosphate ion to retain their viability or whether in some cases the presence of other ions may be necessary.

DISCUSSION

The influence of salt solutions on the viability is entirely determined by the nature of the anions. The addition of phosphate to the solution containing any of the other ions that we studied is sufficient to counteract its deleterious effect. This cannot be compared with the balancing of the Na ions by Ca or K in the fluid used for the perfusion of the surviving heart; in this case both ions are toxic, but their combination is not. In the case of the colon bacilli the phosphate solution does not possess any deleterious effect. On the contrary, we have shown that the presence of phosphate ions is necessary and sufficient for the survival of the colon

bacilli. Part of the harmful effect of the other ions may be due to the fact that they permit the diffusion of the phosphate ions out of the bacteria; this is further confirmed by the fact that the addition of phosphate counteracts to a large extent the action of the other anions. The action of the anions in solutions without phosphate is not entirely due to the absence of the phosphate ion, as is shown by the existence of the series of increasing toxicity: NO_3, Cl^- SO_4, I^- To explain the existence of this series and the action of the phosphates we must, however, assume that the bacilli are permeable for anions. No such assumption is necessary in the case of the kations. The only difference observed was one connected with the valency of the kations. A solution of $CaCl_2$ of the same molecular concentration as a NaCl solution contains twice as many Cl^- ions and must be more toxic. If we decrease the molecular concentration, we decrease at the same time the osmotic pressure below the optimum, and the results must still be more unfavorable than in the case of the univalent ions.

SUMMARY AND CONCLUSIONS

1. The optimum concentration for the viability of the colon bacillus is 1/4 M in the case of nonelectrolytes and 1/8 M in the case of binary electrolytes.

2. The hydrogen-ion concentration in phosphate solutions is of small importance as long as it remains above P_H 5 and below P_H 8.

3. The kations are without effect on the viability of the colon bacillus, except for a valency effect.

4. The series of increasing toxicity for the anions is HPO_4^{--}, NO_3^-, Cl^-, SO_4^{--} I^- Their effect is purely additive; no evidence was found of "balaneing" the toxicity of one ion by that of another.

5. The HPO_4^{--} ion is the only mineral constituent necessary for the life of the colon bacillus. Part of the toxicity of distilled water and salt solutions may be due to the fact that they permit the diffusion of the $HPO_4^=$ ion out of the bacteria.

6. The number of colon bacilli remains constant in a solution containing a mixture of primary and secondary sodium phosphate of P_H 7. The number of bacilli increases if traces of organic material are present in the solution; e.g., cotton fibers or dead bacilli.

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THE RELATIVE TOXICITY OF GENTIAN VIOLET FOR CERTAIN MEMBERS OF THE COLON GROUP OF ORGANISMS*

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THE selective action of gentian violet for organisms having a gram-positive reaction was reported by Churchman, 1912. He studied the bacteriostatic effect of this dye and its relation to the gram reaction of the organism when the dye was added to the media in a dilution of one to seventy-five thousand.

Following Churchman's suggestion, Hall and Ellefeson, 1917, report the use of gentian violet for isolating B. coli from milk. They added the dye to the broth to make a dilution of one to twenty thousand and reported a satisfactory result. They also reported, in 1918 and again in 1919, the use of the same dye in eliminating spurious presumptive tests for B. coli in water analysis. They suggested its use in routine bacteriologic examination of water and said, 1919; "One to twenty thousand gentian violet not only increases the total number of samples from which B. coli can be isolated, but reduces the number of spurious presumptive tests to a minimum." Winslow and Dolloff, 1922, reported the inhibitive concentration of gentian violet for B. coli in lactose broth as one part of the dye in fifty thousand parts of the media.

As a result of these reports we began, in 1924, to use gentian violet in the lactose broth used in the routine testing of water samples for B. coli. We concluded from the literature sighted that the best dilution of dye would be around one to forty thousand. We found that the dye when used in this manner exerted a marked inhibitory effect upon certain strains of B. coli. In 1918 we showed that of 200 cultures of B. coli isolated from as many samples of water, 60 per cent gave a positive Methyl red and negative Voges-Proskauer test. In as much as gentian violet has been recommended for its favorable selective action in isolation of B. coli and inasmuch as our results indicated that the dilution recommended undoubtedly inhibits certain strains, we decided to determine the relative toxicity of gentian violet on cultures of B. coli giving a Methyl red and Voges-Proskauer test.

EXPERIMENTAL WORK

In this work we subjected the cultures described above to various dilutions of gentian violet in lactose bouillon adjusted to P_H 7.0. The effect of the dye was determined by observing gas formation at the end of twenty-four and forty-eight hours' incubation, and by making agar plates from the tubes at these intervals and counting the colonies growing at the end of

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Received for publication, January 20, 1928.

forty-eight hours. The inoculations of the gentian violet lactose bouillon tubes were made as follows: A twenty-four-hour growth on plain agar slants was washed down with two c.c. of sterile salt solution. A loopfull of this suspension was transferred to ten c.c. of sterile salt and shaken well. From this suspension a tube of plain nutrient broth was inoculated with one loopfull and allowed to incubate twenty-four hours. A loopfull of the twenty-four-hour plain nutrient broth culture was transferred to ten c.c. of sterile salt and shaken well. This suspension was used to inoculate the gentian violet lactose broth tubes, using one loopfull to each tube. At the same time a lactose broth fermentation tube without gentian violet was inoculated in a similar manner. The tubes were incubated for forty-eight hours, being observed for gas production after twenty-four and forty-eight hours' incubation. At the same time, twenty-four and forty-eight hours, agar plates were made from each tube and counted after forty-eight hours' incubation. The dilutions of gentian violet in the media ranged from a strength of one part of dye to one hundred thousand parts of media to one part of dye to ten thousand parts of media.

Agar plate counts were made on the suspensions used to inoculate the gentian violet tubes so that we might be sure that the fermentation tubes were receiving a large enough inoculation. While the results of these counts do not appear in the tables, they ranged from five hundred and forty to fourteen hundred colonies to the plate. It seems probable, then, that no fermentation tube in the experiment received an inoculation of less than five hundred and forty bacteria.

The result of the inoculation of the lactose bouillon fermentation tubes containing no gentian violet are not included in the tables. These are omitted because all of the tubes in which the gentian violet was diluted highly (1-100,000) showed gas production in twenty-four hours and acted as a control for the rest of the experiment. However, all plain lactose broth tubes showed gas production in the first twenty-four hours.

RESULTS

Table I shows the results of the agar plate counts. These results show that the dye when diluted one hundred thousand times produced no inhibition, which could be detected by the method used, of either group of organisms. That is, there was always from these tubes a good growth on the agar plates. Sometimes the number of colonies which grew on the plates made from the gentian violet tubes were less than the number which grew on plates made from the plain lactose bouillon, but these differences were small. Table I shows that in a dilution of one to seventy-five thousand, one culture of the methyl red group failed to grow. At a dilution of one to sixty thousand three cultures failed to grow. At a dilution of one to thirty thousand, the dye showed a 90 per cent inhibitory effect, while at a one to fifteen thousand no culture grew.

The result with the Voges-Proskauer reacting organism shows no inhibitory effect until a dilution of one to thirty thousand is reached and then only one to the eight cultures used failed to grow as against a 90 per cent

TABLE I

TABLE SHOWING INHIBITORY EFFECT OF GENTIAN VIOLET LACTOSE BROTH AS INDICATED BY AGAR PLATE COUNTS MADE FROM BROTH AT END OF TWENTY-FOUR AND FORTY-EIGHT HOURS

a. Methyl Red Positive Organisms

	1–100000		1–75000		1–60000		1–40000		1–30000		1–20000		1–15000	
CUL. NO.	24	48	24	48	24	48	24	48	24	48	24	48	24	48
1	540	330	6	580	0	0	0	0	0	0	0	0	0	0
2	580	550	2	600	0	0	0	0	0	0	0	0	0	0
3	1050	360	2	1400	0	14	0	6	0	0	0	0	0	0
4	360	220	0	0	0	0	0	0	0	0	0	0	0	0
5	1050	440	480	1050	980	4200	380	380	0	0	0	0	0	0
6	2100	900	500	840	250	700	6	400	0	0	0	0	0	0
7	1400	1050	0	1750	1	1260	0	0	0	0	0	0	0	0
8	1400	540	15	680	2	1750	0	0	0	0	0	0	0	0
9	2100	750	460	0	880	840	140	350	160	730	0	280	0	0
10	480	280	480	0	640	840	0	0	0	0	0	0	0	0

b. Voges-Proskauer Organisms

11			770	1050	1050	840	360	700	90	360	21	240	1	18
12			840	1050	840	700	510	520	200	370	28	310	5	38
13			540	1400	540	490	300	420	0	0	0	0	0	0
14			940	2100	530	700	320		110	110	0	0	0	0
17			560	460	1050	440	600	380	0	0	0	0	0	0
18			1400	1260	1750	1400	1050	650	1400	1700	96	1260	19	700
19			540	1400	280	560	450	520	320	650	0	52	0	0
20			520	1500	480	490	630	1050	0	270	0	0	0	0

inhibition for the methyl red positive organisms. It is also seen from this table that at a dilution of one to fifteen thousand, the point at which every methyl red organism was prevented from growing, only a 62 per cent inhibition of the Voges-Proskauer organisms was apparent.

A further study of Table I shows that in a one to one hundred thousand dilution of the dye no evidence of lag of the growth was apparent. In this dilution the number of bacteria growing in the tubes after twenty-four hours' incubation as indicated by the number of colonies on the agar plates is slightly greater than after the second twenty-four hours. This was also true of the plates made from the tubes containing no gentian violet. This would seem to indicate that the maximum bacterial growth was reached in these tubes in the first twenty-four hours. From this dilution (1-100,000) down, every dilution, except on cultures 9 and 10, shows an evidence of lag in the first twenty-four hours in the methyl red group. This evidence was more apparent as the amount of the dye in the media was increased.

The organisms of the Voges-Proskauer group do not show this lag until a relatively low dilution (1-30,000) is reached. The counts from the tubes containing the higher dilutions of dye are so nearly alike or are so high both after twenty-four- and forty-eight-hour incubation that no inference can be made by their comparison.

It is apparent that a few of the organisms in each group showed more resistance to the dye than other members of the same group. This is seen by comparing cultures No. 1 and 2 with cultures No. 5, 6, and 9 of the methyl red group. Culture No. 1 began to show marked sensitiveness to the dye in dilution of one to seventy-five thousand, while the other cultures showed

a good growth on the plate until a dilution of one to forty thousand was reached. On the other hand, culture No. 9 was particularly resistive, continuing to grow until a dilution of one to fifteen thousand was reached. The sensitiveness of cultures No. 1 and 2 is also seen by a comparison of the twenty-four- and forty-eight-hour counts from the tubes containing a one to seventy-five thousand dilution of gentian violet. This shows that after twenty-four hours' incubation, the plates from these tubes grew only six colonies while from these tubes at the end of forty-eight hours, the plates grew 580 colonies. This is interpreted to mean an inhibition by the dye causing a lag in the growth of the organisms for the first twenty-four hours.

Table II shows the effect on gas production from lactose by cultures of B. coli when gentian violet is added to the lactose bouillon.

TABLE II

SHOWING THE EFFECT OF VARIOUS CONCENTRATIONS OF GENTIAN VIOLET ON CULTURES OF B. COLI AS EVIDENCED BY THE PRODUCTION OF GAS* IN GENTIAN VIOLET LACTOSE BROTH

Twenty-Four Hour Gas Production

CONCENTRATION GENTIAN VIOLET	POSITIVE METHYL RED ORGANISMS										NEGATIVE VOGES-PROSKAUER ORGANISMS							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	17	18	19	20
1 to 100,000	+	+	+	+	+	+	+	+	+	+	−	−	−	−	−	−	−	−
1 to 75,000	0	0	0	0	+	+	0	0	0	+	+	+	+	+	+	+	+	+
1 to 60,000	0	0	0	0	0	0	0	0	0	0	+	+	0	+	+	+	0	0
1 to 40,000	0	0	0	0	0	0	0	0	0	0	+	+	0	+	+	+	0	+
1 to 30,000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	0	0
1 to 25,000	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1 to 20,000	−	−	−	−	−	−	−	−	−	−	0	0	−	0	0	0	0	0
1 to 15,000	−	−	−	−	−	−	−	−	−	−	0	0	−	0	0	0	0	0
1 to 10,000	−	−	−	−	−	−	−	−	−	−	0	0	−	0	−	0	0	0

Forty-Eight Hour Gas Production

1 to 100,000	+	+	+	+	+	+	+	+	+	+	−	−	−	−	−	−	−	−
1 to 75,000	+	0	+	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1 to 60,000	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+
1 to 40,000	0	0	0	0	+	+	0	0	+	0	+	+	+	+	+	+	+	+
1 to 30,000	0	0	0	0	0	0	0	0	+	0	+	+	0	+	0	+	+	+
1 to 25,000	0	0	0	0	0	0	0	0	0	0	+	+	0	+	0	+	+	+
1 to 20,000	−	−	−	−	−	−	−	−	−	−	0	+	−	0	0	+	0	0
1 to 15,000	−	−	−	−	−	−	−	−	−	−	0	0	−	0	0	+	0	0
1 to 10,000	−	−	−	−	−	−	−	−	−	−	0	0	−	0	−	0	0	0

*5 per cent or more was considered gas formation.

These results were observed in the same tubes from which the agar plate counts were made and the results are recorded so that the cultures have the same number. A study of this table shows that all of the methyl red cultures produced gas in the first twenty-four hours in the tubes containing the dye in a dilution of one to one hundred thousand, and that all but 3 failed to produce gas in the first twenty-four hours when exposed to the effect of the dye in a dilution of one to seventy-five thousand. There was a complete absence of gas in all methyl red organisms in the first twenty-four hours' incubation in the presence of the dye in the proportion of one part of dye to sixty thousand parts of media. This table also shows what the bacterial counts showed, i.e., that in the case of the methyl red organisms the gentian violet produced a period of lag after which growth takes place faster. The methyl red positive organisms show this more than the Voges-Proskauer organisms. Evidence of this is seen in the table by an absence of twenty-four-hour gas production, and its production in forty-eight hours in many of the cultures. It is also apparent from this table that some cultures are more resistant to gentian violet than others. This is evidenced by cultures 5, 6, and 9 which continued to produce gas in forty-eight hours after the others had been completely inhibited. These are the same organisms which showed stronger resistance by the plate counts.

The organisms of the Voges-Proskauer positive group were not inhibited as evidenced by gas production until a dilution of one to sixty thousand was reached, when three cultures (13, 19, and 20) failed to produce gas in the first twenty-four hours. In this group there is no general lag effect, as evidenced by an absence of twenty-four-hour gas until the dilution of the dye had reached one to thirty thousand.

SUMMARY

Gentian violet has a marked inhibitory effect on the growth of B. coli in a dilution of one to twenty thousand. In this strength it prevented growth in 90 per cent of the methyl red and 50 per cent of Voges-Proskauer cultures used in our tests. The inhibitory effect was evident on the methyl red positive cultures in a dilution as high as one to seventy-five thousand, while it appeared not to affect the Voges-Proskauer positive group until a very much lower dilution (1-30,000) was reached. The inhibitory action is noticed in the higher dilutions by the lag produced in the growth of the cultures. This lag effect is seen in the methyl red positive in much higher dilutions than in the Voges-Proskauer positive cultures. There is a marked difference in the resistance of the two groups of organisms (methyl red and Voges-Proskauer) to the dye. Within the same groups there is a variation in sensitiveness of the the organisms to the action of the dye.

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HEMOLYTIC ICTERUS RESEMBLING PERNICIOUS ANEMIA*

By Wm. Allan, M.D., Charlotte, N. C.

HEMOLYTIC icterus at times produces remarkable blood pictures that make diagnosis difficult. We have previously reported a case[1] in which the blood picture following an almost fatal hemolytic crisis resembled a combination of myeloid leucemia and pernicious anemia. Krumbhaar[2] points out that the cases with severe anemia may so resemble pernicious anemia that differentiation is difficult, as in the case here presented.

Case history.—A white farmer, aged 31, single, was referred to me April 28, 1924, by Dr. A. F. Thompson of Troy, N. C. This young man looked about sixteen years old, was tall, thin, and ghastly pale with lemon tinted skin and with deeply bronzed face and hands; he was very weak and short of breath; and his ankles were considerably swollen. He gave a history of paleness and weakness for eighteen years, following whooping-cough at thirteen, but later his father said he had been pale long before that. From the age of fourteen to nineteen he had a breakdown every summer for five years, and for the next twelve years he had a breakdown about every second year. The present breakdown in health dates back about four months during which time he has had every ten days to two weeks headaches and bilious attacks which seem to hold him back. There is no history of any jaundice or anemia in parents, sibs or other members of the family, and the father and several sibs that were seen from time to time showed no evidence of jaundice or anemia so far as inspection went, nor did they have palpable spleens. The only history of weakness before the patient's chronic trouble started is that of several attacks of bloody flux. Physical examination showed dull, muddy looking conjunctivae but no distinct jaundice although the skin had a noticeably yellowish tinge with deep brown pigmentation of hands and face. The throat and lungs were clear. Heart size and sounds were normal, regular, rate 90. Blood pressure 105/50. Abdomen full with thin walls; spleen extended to the crest of the ilium with sharp edge, smooth surface, and not tender. The lower edge of the liver was just palpable. Reflexes normal with very poor musculature and nutrition. Blood examination showed hemoglobin 30 per cent, red cells 1,352,000 giving color index of 1.1; leucocytes 6,300, with polynuclears 72 per cent, lymphocytes 25 per cent, eosinophiles 1 per cent, basophiles 1 per cent, myelocytes 1 per cent. The red cells showed very marked variation in size, shape and staining reaction and a moderate number of normoblasts were seen. In testing the red cells for fragility hemolysis began at 0.40 per cent and was complete at 0.32 per cent salt solution. The blood serum was slightly positive for bile. The urine was strongly positive for urobilinogen, but otherwise negative. The patient seemed too weak and short of breath to justify analysis of the gastric juice.

This hemolytic anemia starting in early youth and running a course marked by remissions and exacerbations for two decades suggested pernicious anemia; but as only about 1 per cent of pernicious anemia begins so early in life,[3] and as only about the same proportion[3] has very large spleens, this diagnosis did not seem probable. On the other hand, the negative family history and the lack of increased red cell fragility made the diagnosis of hemolytic icterus too uncertain to advise splenectomy in a very poor surgical risk.

*Received for publication, January 18, 1928.

Blood transfusion followed by iron and arsenic and increased diet for six weeks accomplished nothing as the blood picture on June 11 was practically the same as when first seen. It was evident that a continuation of symptomatic treatment was useless.

The only chance of removing the cause, or at least the locus, of the hemolysis here seemed to be by splenectomy, as the beneficial effects of this measure in both the familial and acquired types of hemolytic jaundice are well known. The lack of the pathognomonic increased fragility of the red blood cells in this case was considered explicable by the observations of Giffin and Sanford[4] that "the increased fragility of hemolytic jaundice can be modified by long continued anemia even to the degree that an increase of resistance may be present."

After two transfusions this large spleen was rapidly removed by Dr. A. G. Brenizer, June 17, and the patient made a good surgical recovery. By the end of the month the hemoglobin had reached 65 per cent and the red cells were 4,336,000. In October, 1924, the patient showed a ruddy skin with a gain of twenty pounds in flesh and a corresponding gain in strength. Early in 1926, his hemoglobin was 84 per cent, red count 6,400,000, leucocytes 15,000, with polynuclears 66 per cent, lymphocytes 30 per cent, eosinophiles 3 per cent, basophiles 1 per cent.

A case of severe hemolytic jaundice of long duration strongly resembling pernicious anemia is reported in which the usual increased erythrocyte fragility was possibly counteracted by long-continued anemia.

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LABORATORY METHODS

USES OF THE BIOLOGIC COLORIMETER AS A STAND FOR THE HAND SPECTROSCOPE*

By Julian D. Boyd, M.D., Iowa City, Iowa, and Victor C. Myers, Ph.D., Cleveland, Ohio

IN THE quantitative estimation of certain substances, methods have been employed which are based upon the extinction of spectral bands by dilution. The accuracy and delicacy of such determinations are not dependable, due to the absence of a standard degree of illumination, and the change of characteristics of the absorption spectrum upon dilution. It is preferable to use solutions of similar concentrations in any series of comparable analyses. The spectral intensity can be determined by varying the thickness of the layer of liquid which is interposed between the slit of the spectroscope and the source of illumination, using as an end-point either the point of disappearance of the absorption band, or by matching its intensity with that of a standard solution set at a suitable depth of liquid.

For several years one of us has been using a modified colorimeter for this purpose. The first model, described in this journal[1] was soon superceded by an adaptation of the Duboscq colorimeter, which had a greater range of applicability. The eyepiece of the Duboscq (Pellin) colorimeter was temporarily removed, and a hand spectroscope inserted in its place. By exposing the prisms and sliding them to one side so that the dividing line just passes out of the field of vision and the light comes entirely through one cup, a single spectrum is obtained, while by leaving the prisms in their regular position and adjusting the spectroscope so that the spectrum is vertical to the field of vision, two spectra will be seen lying side by side. Recently Bausch and Lomb have constructed two instruments for us which are an outgrowth of this earlier instrument employed by one of us (B).

In the first of these instruments (see Fig. 1) designed by Myers, the eyepiece and prisms of a B. and L. biologic colorimeter were replaced by a hand spectroscope on a special mounting. The spectroscope has a fixed aperture and a metal eyeshield. The two plungers and cups of the colorimeter are replaced by a single plunger and cup, which together with the rack and pinion are centered directly below the spectroscope. This is a particularly convenient mounting for a hand spectroscope, since the concentration at which characteristic absorption bands occur may be almost instantaneously obtained by raising or lowering the cup. When a solution showing absorption bands,

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Received for publication, October 1, 1927.

for example oxyhemoglobin, is placed in the cup, the variations in these absorption bands may be quickly studied by raising and lowering the cup, also the disappearance point of the absorption bands may be readily determined. When the disappearance of absorption bands is made the basis of a quantitative method, as for example in the spectroscopic estimation of urobilin, this instrument is a very convenient one to use. With constant intensity of illumination and a similar initial dilution, successive results are comparable and quite accurate.

The second of these instruments (see Fig. 2) was designed by Boyd as an accessory attachment for the standard colorimeter. By replacing the eyepiece of the latter with this adaptation, the instrument becomes a spectro-

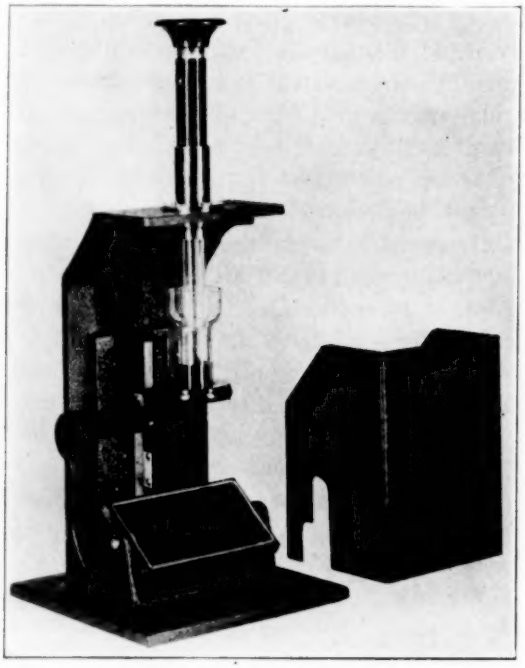

Fig. 1.—Hand spectroscope mounted on stand of B and L biologic colorimeter.

comparator. The adapter consists of a hand spectroscope mounted in a tube which is of the same diameter as the eyepiece; it is equipped with an accessory lens which increases the spectral dispersion. The spectrum lies vertical to the plane of vision, the red field being uppermost. Light entering the instrument through the two glass plungers gives rise to two spectra lying side by side, as readily comparable as are the two fields of the colorimeter. The instrument may be used as the one described above, using the blank side as a control. Greater accuracy can be obtained, however, by using a standard solution of known concentration in one cup, set at a suitable depth, and matching the intensity of the bands of the unknown solution with this. As it is necessary to shield the eye from other sources of light while using the instrument, a special rubber eyeshield has been devised for this purpose.

In comparison with the instrument shown in Fig. 1, the spectrocomparator has two important advantages, (1) that a special instrument is not required, since the conversion from a colorimeter to a spectrocomparator (Fig. 2) or vice versa requires only a few seconds, and (2) that a control spectrum or the absorption bands of a standard are always in the same field of vision with the unknown. It has the disadvantage that the spectrum field observed is considerably smaller. For purely qualitative work the instrument shown in Fig. 1 is probably preferable.

Fig. 2.—The spectrocomparator; an adapter for the colorimeter.

As a quantitative clinical method the spectroscopic method of measurement has been used chiefly in the estimation of urobilin by the Wilbur and Addis technic. In the estimation of hemoglobin it checks quite well with the colorimetric methods. It would seem quite applicable to the determination of any substance yielding definite absorption bands, even in the presence of colored contaminants, provided that the absorption spectrum is not obscured.

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THIOCYANATE AS A SOURCE OF ERROR IN THE FERRIC CHLORIDE TEST FOR LACTIC ACID, WITH A METHOD FOR THE ELIMINATION OF THE THIOCYANATE*

By Lathan A. Crandall, M.S., Chicago, Illinois

IN THE course of routine tests for lactic acid in human gastric juice, it was found that in many individuals a thiocyanate was present in the samples, and that this was a source of error since it gave a color with ferric chloride somewhat similar to that given by lactic acid. Since this must be a very common contamination, and since it is not mentioned in those texts on Clinical Diagnosis which were consulted, it appeared advisable to call attention to this source of error and to a method by which it may be avoided.

KCNS is commonly present in human saliva. Schneider[1] tested 225 cases and in only one did he find no KCNS. He found it to be present in greater concentration in the saliva of smokers than in that of nonsmokers. Kelling[2] reports that he found KCNS in the gastric secretion. In very small concentrations KCNS gives with ferric chloride a yellow color somewhat more brown than that given by lactic acid. In greater concentrations the KCNS gives a brown or brownish red which may entirely obscure any yellow lactic acid color. Thus it is a source of error both by simulating the lactic acid color and by obscuring it.

While KCNS is generally known to be present in saliva, it is not generally recognized as a constituent of gastric juice. Tests on the gastric contents of human subjects were carefully made to avoid any contamination of the gastric secretion by saliva (the saliva was expectorated and none was consciously swallowed) and still KCNS appeared in the gastric contents. No quantitative tests were made, but the concentration in gastric juice seemed to be less than in the saliva of the same individual. In order to be sure that the gastric secretion was not being contaminated by KCNS bearing fluids from the mouth or duodenum, a Pavlov pouch dog was injected subcutaneously with 0.1 gram of NaCNS after the gastric glands had been stimulated by a meal of meat, and the KCNS content of the gastric juice was followed at half hour intervals. One-half hour after the injection of the NaCNS the gastric juice gave a very faint test for KCNS; one hour after the injection the test was very strong, and one and one-half hours after the injection it was still quite marked.

It was found that the KCNS could be precipitated by the heavy metals, and that the best substance for this purpose is $HgCl_2$, in saturated solution. I later found that Kelling[2] had previously used the same method for the elimination of KCNS.

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Received for publication, November 13, 1927.

Elimination of KCNS by $HgCl_2$ solution is applicable to any of the common tests for lactic acid. A saturated solution of the mercury salt is used. If saturated $HgCl_2$ be added to a solution of KCNS no color is present, and on the further addition of ferric chloride the solution takes on only the very faint brown caused by the ferric chloride itself. If lactic acid and KCNS are present in the same solution, there is no change in color on the addition of a saturated solution of $HgCl_2$, but on the addition of ferric chloride the typical lactic acid color develops. If Uffelman's test is used, the gastric content is treated with an equal amount of saturated $HgCl_2$ before adding it to the Uffelman's reagent. If Strauss' test (extraction with ether) be used, the elimination of thiocyanate is equally as important as with the more simple tests, since the thiocyanates are very soluble in ether. If an amount of saturated $HgCl_2$ solution equal to that of the solution to be tested is added prior to the ether extraction, the extract will be free from KCNS.

The addition of $HgCl_2$ in no way decreases the sensitiveness of the test for lactic acid except as it dilutes the material to be tested. If the material to be tested is neutral or alkaline, it should be made acid with HCl before the addition of the $HgCl_2$; this serves the double purpose of liberating lactic acid from the proteins and avoiding precipitation of mercury by alkali.

It is hoped that this method of avoiding a common source of error, especially in patients who smoke, will increase the value of the test for lactic acid. The organic acids and the fatty acids still remain as contaminations. However, they are not usually found in the stomach following the test meal unless fermentation is taking place.

SUMMARY

It is pointed out that KCNS is a common and generally unrecognized contamination in the ferric chloride test for the presence of lactic acid in gastric contents, and may lead to incorrect conclusions especially in patients who smoke. It is shown that KCNS is secreted by the gastric glands. The addition of saturated $HgCl_2$ solution prior to the performance of any of the common tests for lactic acid will remove the KCNS.

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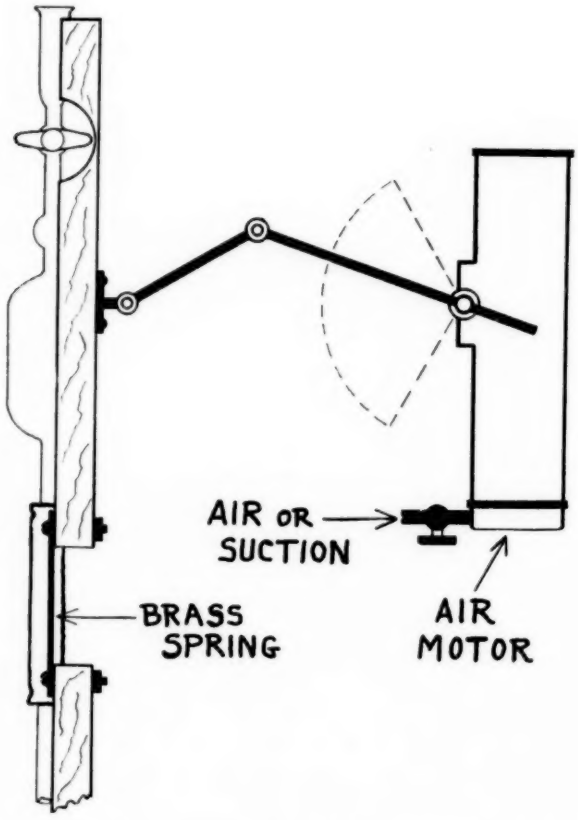
AN INEXPENSIVE SHAKER FOR THE VAN SLYKE BLOOD-GAS APPARATUS*

By H. F. Pierce, Baltimore, Md.

SINCE the Van Slyke blood-gas apparatus of the constant volume type is now almost universally employed in hospitals and other medical institutions, the simple and inexpensive shaking device here illustrated may be of interest to technicians and other users of the apparatus.



As is shown in the diagram, the gas bulb is mounted on a board, which is attached to the frame supporting the rest of the gas apparatus by two narrow strips of thin spring brass, one on either side of the rubber connecting tube. To the back of the board carrying the gas bulb is attached a jointed connecting rod, the far end of which is fastened to the shaft of a reciprocating air motor such as is commonly used to operate automobile windshield wipers.

*From the Wilmer Ophthalmic Institute, The Johns Hopkins Hospital.
Received for publication, November 21, 1927.

The connecting rod should be mounted so as to swing through the arc indicated by the dotted lines in order to obtain the maximum shaking effect. Power for the air motor is obtained from the suction of a large water aspirator of the usual kind. A similar motor designed to operate on compressed air is on the market, and may be used if the laboratory is provided with air mains. In choosing a suitable motor, care should be taken to select one powerful enough to do the work.*

Apparatus fitted with this device has been in use for over a year, and has yielded results which check with those secured from a similar apparatus provided with an electric motor shaker.

A SIMPLE AND EFFICIENT APPARATUS FOR THE DISTILLATION OF UREA NITROGEN†

By Lyman C. Murphy and Robert C. Jenkins, Chicago, Ill.

WHILE it must be acknowledged that the distillation method of Folin and Wu for the determination of urea nitrogen is more accurate and expeditious than aspiration, many technicians have discarded the former method for the latter, owing to the difficulty of preventing the liquid in the receiving tube from sucking back, or to the tendency of the solutions in the distilling tube to froth over.

We have found that by constricting the delivery end of the connecting tube, thereby maintaining a gentle but fairly uniform pressure within the apparatus, the frothing is restricted, and so long as the flame is shielded and not tampered with, there is no sucking back. We are now using, with uniform success, an apparatus which can easily be constructed in any laboratory, using the following or similar materials:

1 small iron support, 18 inches high, rectangular base
1 iron retort ring, 5 inch diameter
1 iron retort ring, 3 inch diameter
2 burette clamps
1 five-inch wire gauze square
1 micro-burner
1 empty ether can (1-pound size)
1 round pyrex flask, 100 c.c. capacity, 15 mm. neck
1 No. 0 rubber stopper
1 piece glass tubing, 7 mm. inside diameter, 24 inches long
1 Folin blood-sugar tube

The center of the 7 mm. glass tubing is heated over a bat-wing burner and drawn out about eighteen to twenty-four inches, then reheated and

*The motors used by the author were supplied by the Folberth Auto Specialty Company, of Cleveland, Ohio, which manufactures both suction and pressure types.

†From the National Pathological Laboratory, Chicago.
Received for publication, December 10, 1927.

separated at the center in the same manner as capillary pipettes. Each piece is now marked with a file across the constricted portion, six inches from the beginning of the constriction, broken off square, and the edges smoothed off slightly in the flame. Two bends are made as shown in the illustration, the first bend beginning not less than eight inches from the small end. The No. 0 stopper is bored to fit snugly over the large end of the tube.

The bottom is cut out of the ether can, so that when it is inverted the micro-burner can pass through the small opening in the top. The apparatus

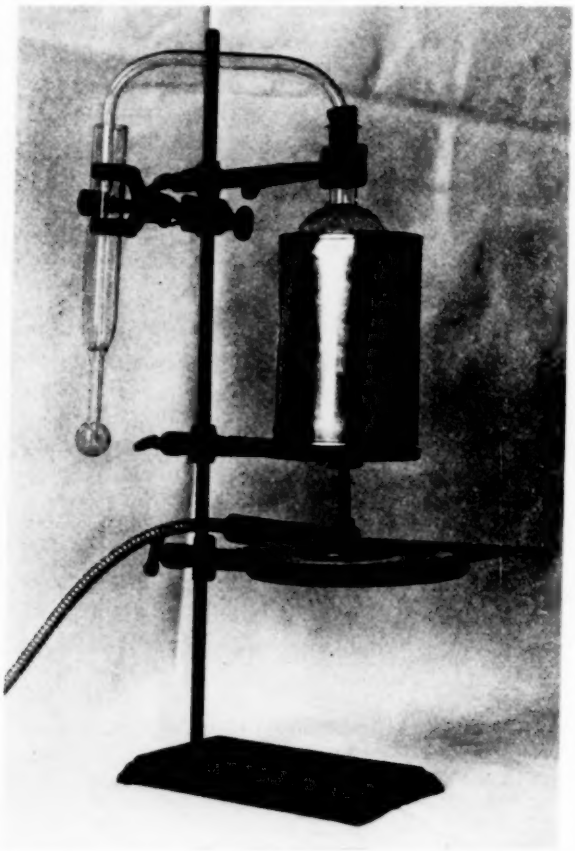


Fig. 1.—Apparatus in position ready to begin distillation.

is now assembled as shown in Fig. 1. The advantage of using the Folin blood-sugar tube as a receiver is the fact that the steam issuing in a fine stream near the bottom must pass through a column of liquid about an inch and a half in height, insuring more complete absorption of ammonia than when a plain tube of greater diameter is employed. This tube is graduated at 25 c.c.

We incubate 5 c.c. of blood filtrate with 1 c.c. of urease solution and two drops of buffer mixture in the 100 c.c. flask, for ten minutes at 40° to 50° C., then add 2 c.c. of saturated borax solution and one drop of caprylic alcohol (to prevent frothing until steam pressure is generated), adjust the

stopper with bent tube attached, so that the bottom of the constricted portion almost reaches the bottom of the Folin sugar tube, which contains 2 c.c. of twentieth normal acid and one or two cubic centimeters of water, place the ether can shield around the flask, and insert the micro-burner, with a low flame (about 1¼ inch to tip) through the neck of the can, allowing the tip of the flame to come within about one-half inch of the bottom of the flask.

No further attention is required until the liquid in the receiving tube has begun to boil. After this boiling has continued vigorously for at least

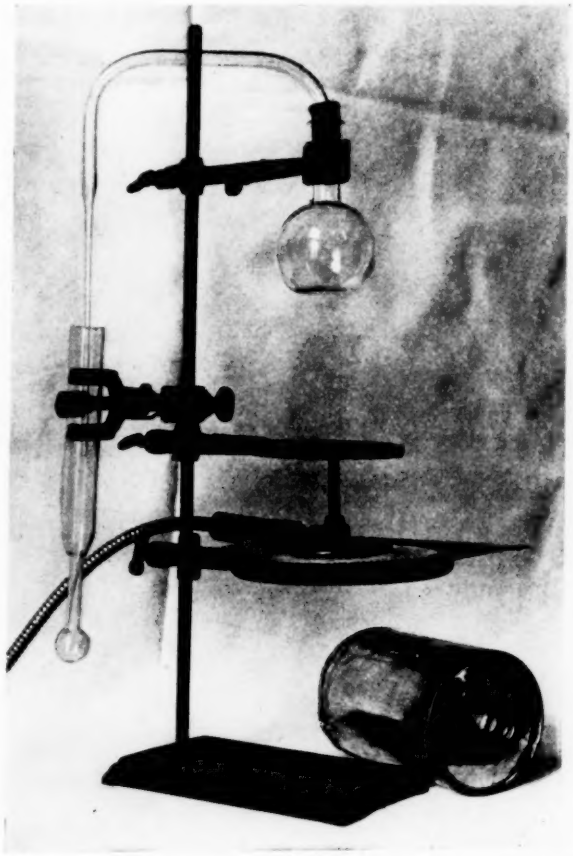


Fig. 2.—Receiving tube drawn down at end of distillation. Ether can removed to show distilling flask.

one minute, or until all traces of the caprylic alcohol (which will be noted condensing in little droplets in the upper portion of the tube) have disappeared, the lower burette clamp is released by loosening the thumb-nut and drawn down until the surface of the liquid in the receiver is well below the end of the constricted tube, the boiling is allowed to continue one minute longer, and the gas turned off.

The receiving tube is now removed and a little distilled water added, allowing room for 2½ c.c. of Nessler's solution, which is added as soon as the contents are cooled, and the volume made up to the 25 c.c. mark.

THE VARIABLE PARTIAL SOLUBILITY OF BASIC FUCHSIN IN ALCOHOL*

By H. W. Wade, M.D., Manila, P. I.

A STOCK alcoholic solution of basic fuchsin is employed in one of the two common methods of preparing the carbol-fuchsin stain. The method referred to is to be preferred as decidedly the more convenient, provided it will give reasonably uniform results. The fact is that, as usually prepared, the stock solution is not a dependable factor as regards concentration. Variations may be so great that they may very well affect the accuracy of findings. In any case, such irregularities, beyond those that are unavoidable in the use of dyes as now sold, are certainly not desirable.

There is no definite standard for the stock dye solution, though it is usually called "saturated." Most writers pay no special attention to its preparation, or its final concentration. A belief exists that the saturation point of fuchsin in 95 per cent alcohol is 3 per cent,[1] and Eyre[2] directs that 3.5 grams be used per cent, with subsequent filtering. Very different is a method for preparing saturated dye solutions in general by which, to begin with, a container is one-quarter filled with the dry substance and then filled with alcohol.[3] When tested in a 100 c.c. cylinder this method took 15.2 grams of fuchsin and 88 c.c. of alcohol.

Undoubtedly, the usual procedure for preparing the stock solution is simply to add dye "in excess" to the desired quantity of alcohol. This involves an assumption that solution is complete, or practically so, until a saturation point is reached. In so far as the lot of fuchsin in our stock† is typical of this dye in general, this assumption is erroneous. This fact (or, if it be not constant, this possibility), however, well known to dye technologists, is not available to the medical laboratory worker in the texts commonly used by him.

EXPERIMENTS

Several systematic experiments on the matter were made following an observation that two stock alcoholic solutions prepared by the ordinary "substance-in-excess" method differed grossly in apparent density. Different grades of alcohol (absolute, 95 per cent and 80 per cent) were used in the tests, a preliminary one having shown that solubility varied considerably with the strength of the alcohol.

The various solutions were prepared in rubber-stoppered test tubes, using in each instance 10 c.c. of alcohol. They were repeatedly agitated and kept

*From the Culion Leper Colony, Philippine Health Service.

Received for publication, November 25, 1927.

†The findings here reported were obtained with a lot of dye manufactured by the Coleman and Bell Company (Lot No. 780, labelled "Pure Crystals" and "certified" by the manufacturer to be 99.8 per cent soluble in water and 99.9 per cent in alcohol), and supplied by the Arthur H. Thomas Company, Philadelphia; it is entirely satisfactory in use, both in staining and in the Endo medium.

slanted to obtain maximum exposure to the solvent. On the following day 5 c.c. of the fluid was removed for drying, usually by pipetting after centrifuging. Usually the solutions were effected at room temperature, which ranged from 25 (night) to 32 to 34 (day), but in observing crystallization one extensive set was heated to 57° C. and then chilled; before sampling they were again warmed to about 40° C.

The results obtained, in grams of substance recovered per 100 c.c. of actual solution, are given in Table I, and the curves derived from these figures in Fig. 1. The curves are straightened somewhat; the figures actually obtained reflect the influence of the small quantities used, among other things, but the inaccuracies are unimportant.

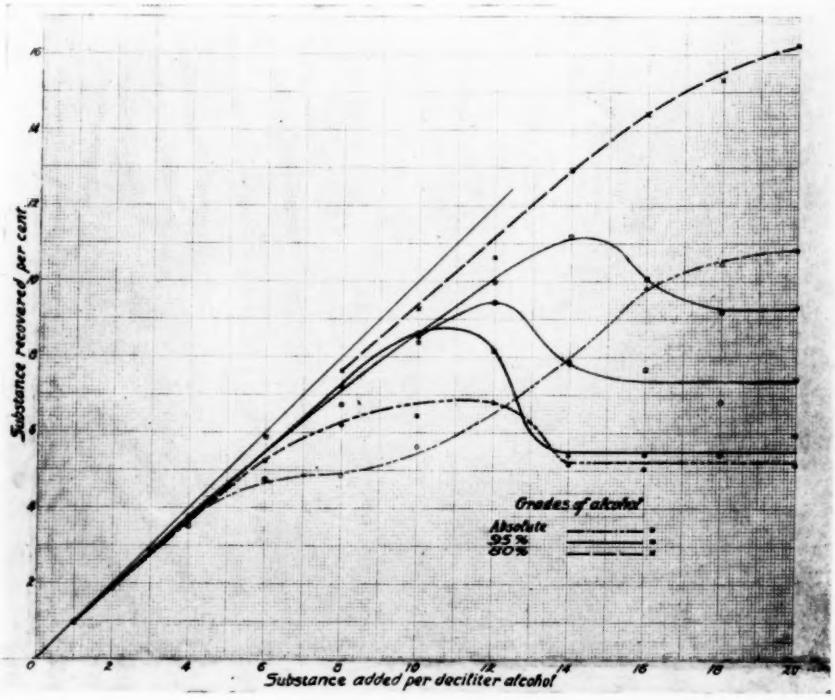


Fig. 1.—Solution-curves of the lot of basic fuchsin tested, in absolute, 95 per cent and 80 per cent alcohols. The heavier lines (including the single 80 per cent curve) are of the room temperature tests, the lighter ones the heated tests.

DISCUSSION OF RESULTS

In none of the proportions used was the dye completely dissolved. Even with as little as 1 gram per 100 c.c. of 95 per cent alcohol there was some residue, and with 2 or 3 grams, this was sufficient perhaps to satisfy an inexperienced person that the solution was saturated. This was far from the case. In the proportion of 10 grams of substance to 100 c.c. of alcohol the concentration of substance (or substances) dissolved amounted to about 8.5 per cent. The idea that 3 per cent is the concentration of saturation of basic fuchsin in alcohol is, at least sometimes, far from correct.

The reason for the variable partial solubility shown is not clear. The

TABLE I

CONCENTRATION OF ALCOHOLIC SOLUTIONS OF BASIC FUCHSIN

GRAMS DYE PER CENT ALCOHOL	STRENGTH OF ALCOHOL AND TEMPERATURE					
	ABSOLUTE		95 PER CENT			80 PER CENT
	ROOM	HEATED	ROOM	HEATED (1)	HEATED (2)	ROOM
1	0.99	1.00	0.96	0.94	–	–
2	1.85	1.90	1.88	1.80	–	–
3	2.80	2.86	2.86	2.84	–	–
4	3.60	3.78	3.50	3.74	–	–
6	5.24	4.72	4.74	5.88	–	–
8	6.20	4.86	7.20	6.76	–	7.62
10	6.44	5.62	8.60(a)	8.38	8.52	9.26
12	6.80	6.78	8.15(b)	9.96	9.44	10.62
14	5.40	7.82	5.18	11.16	7.86	12.94
16	5.04	9.80	5.38	10.08	7.66	14.42
18	5.40	10.45	5.38	9.18	6.80	15.32
20	5.14	10.72	5.94(c)	9.28	7.40	16.24

(a) Average of 2 findings, 8.80 and 8.40.
(b) Average of 2 findings, 8.62 and 7.68.
(c) In another test, 6.74.

Stains Commission points out[4] that variations in the inert materials used to dilute dye powders affect the amount of dye that will dissolve, wherefore they no longer recommend the use of "saturated solutions" in formulas. But this refers to differences in the maximum solution-concentrations of different lots of dye, not to the condition here discussed. If it be that the relatively small amount of diluent present in one or two grams prevents complete solution when with ten grams total concentration of 8.5 grams is obtained, this indicates marked sensitiveness on the part of some fraction of the dye.

It may be that this is the explanation, and that the curve is due to gradually increasing effect of a mixed dye-diluent solution on the more sensitive portion. It is recognized that basic fuchsin as marketed is a more or less variable mixture of rosanilin homologues, though it would seem that the number of fractions that should be present in any case is not large; indeed, a given lot may be a single chemical entity, as the monomethylated compound (rosanilin), or that with three methyl radicals (new fuchsin).[5] It would be of interest to compare the solubilities of lots of dye of known constitution. It may be noted that staining tests made to compare undissolved and dissolved fractions showed no important difference.

In most of the series a crystalline slush (*brei*) formed at and beyond a certain point of dye-concentration. The crystalline mass was often so bulky as to cause actual solidification. The fluids recovered after crystallization appeared to be truly saturated (flattened curves), though they contained considerably less substance than those below the crystallization-point. Crystallization is apparently not dependent on ordinary supersaturation; it occurs spontaneously, at rising room temperatures, in the presence of an abundance of undissolved dye. It has been suggested to me that in this process alcohol may have been taken up as alcohol of crystallization. It seems uncertain whether the crystals are of dye or of its diluent. However, this is somewhat foreign to the interests of the user of biologic stains.

A feature to be mentioned in passing is that, though the solubility of the dye in pure water was very low (much below 1 per cent), increased water content of the alcohol, within the limits used, greatly increased its capacity to take up the dye. This is striking for 80 per cent alcohol, and it was expected that a 10 per cent stock solution in it would be satisfactory for actual use, but staining solutions made from it appeared turbid, and they stained the bacilli (of leprosy) an unattractive dull red. Another feature is that the sets that had been moderately heated attained (and retained after crystallization when this occurred) higher concentrations than the others. However, this obtained only in the tubes containing the larger quantities of dye, larger than those required for staining purposes.

It is evident that stock alcoholic solutions should be prepared with a weighed quantity of dye. Ten grams per 100 c.c. of 95 per cent alcohol gave fairly uniform results in four tests, the concentrations ranging from 8.38 to 8.80, with an average of 8.54 per cent. This concentration is such that carbol-fuchsin made by adding 10 c.c. of this solution to 90 c.c. of carbolic solution is probably about equal in dye content to that made by adding 1 gram of the same powder to 100 c.c. of the carbol water plus 10 c.c. of alcohol, and filtering off the undissolved residue. This stock solution has in the past year or so proved entirely satisfactory. In the interest of uniformity it is probably best that the residue be not allowed to accumulate in the stock bottle.

SUMMARY AND CONCLUSIONS

In solubility tests a good commercial sample of basic fuchsin has not gone completely into solution in amounts below the limits of solubility. There is an undissolved residue even in the lower suspension-concentrations used. There is, therefore, no definite saturation point in the usual sense of this term. The residues are not uniformly proportional to the amounts of substance used, but tend to increase in proportion.

Other features observed are that sooner or later in a test series spontaneous crystallization occurs; that moderate heating causes a distinct increase in the amounts dissolved and held in solution; and that though the solubility of the dye in water is low, solubility in alcohol increases with its water content. However, these features need not concern the user of the dye in staining.

The main observations, which recent tests with certain other dyes show to be not unique, constitute a further reason for abandoning the use of "saturated" solutions made by the substance-in-excess method. Of the dye tested, solutions made from 10 grams per 100 c.c. of 95 per cent alcohol, which are of approximately 8.5 per cent concentration, have proved entirely satisfactory for making carbol-fuchsin stain.

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[4]Conn, H. J., et al.: Biological Stains, Commission on Standardization of Biological Stains, Geneva, New York, 1925, p. 24.
[5]Conn, H. J., et al.: Biological Stains, Commission on Standardization of Biological Stains, Geneva, New York, 1925, p. 62-65 and 133.

TWO METHODS FOR THE EOSINOPHILE COUNT IN THE COUNTING CHAMBER FOR ROUTINE WORK*

By Akira Sato, M.D., Sendai, Japan

THE differentiation of eosinophiles is, of course, very important in routine blood counts. One may thus be led to suspect infestation with animal parasites, in spite of negative stool findings.

This paper deals with two methods for routine use. The first is for the eosinophile count only. The second is for the recognition of eosinophiles in the counting chamber when stained by peroxidase reaction (copper method). With a little practice one will be able to estimate the number of eosinophiles while making a differential count.

1. *Method for Eosinophiles Only.*—This method is not original, but only a slight modification of the excellent Dunger Method.[1] Our experience is that the stain made according to his directions lasted only one or two weeks, after which it became turbid.

PROCEDURE

Two solutions are required:

Solution I. One per cent water soluble eosin. (Grubler) 20 c.c.

Solution II. (for Eosinophile).
Acetone 80 c.c.
Distilled water up to 400 c.c.

Before using, mix one part of Solution I and four parts of Solution II. Draw the blood to the mark, then fill with the solution up to the mark 11. The fluid is then introduced into the counting chamber. The concentration of eosin is very low compared with that in the original method, but it is very satisfactory.

2. *Eosinophile Count by the Peroxidase Reaction.*—The second method was not originally designed for counting eosinophiles, but to differentiate

*From the Department of Pediatrics, Faculty of Medicine, Tohoku Imperial University, Sendai, Japan.
Received for publication, December 2, 1927.

lymphatic and myeloid cells in the counting chamber. However, when one has acquired some practice with the method of Sato and Shoji[2] one will be able to count monocytes separately from the other myeloid elements, because they will appear red with the low power objective, although they contain blue granules distinctly recognizable with the medium power objective. The eosinophiles are a dark blue among the lighter blue neutrophiles when seen with the low power objective. In Table I is given the eosinophile counts by this method and also by method I described above.

The results of the two methods give good agreement. The second method thus gives a rough estimate of the eosinophile count, with no extra time or trouble. Tokue in our laboratory will report further in the near future.

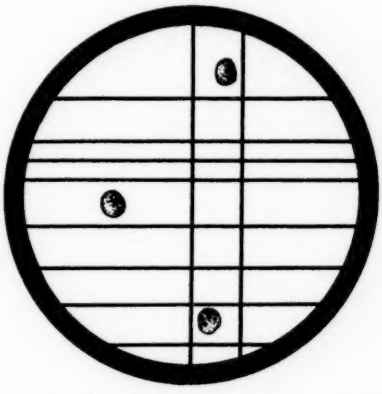

Fig. 1.—The eosinophile count in counting chamber.

TABLE I

	COUNTING CHAMBER PEROXIDASE METHOD		MODIFIED DUNGER METHOD
INFANTS	TOTAL LEUCOCYTE COUNT	SUSPECTED EOSINOPHILE CELLS IN PERCENTAGE	EOSINOPHILE CELLS IN PERCENTAGE
Case I (Saijo)	10900	2	2
Case II (Kanemoto)	8000	4	4
Case III (Kikuchi)	5080	16	15
Case IV (Oikawa)	3630	4	4
Case V (Kaneda)	7820	14	13

SUMMARY

Two methods for counting eosinophiles are described. One is a modification of the Dunger method with permanent reagents. The second is the counting chamber method of the peroxidase reaction (copper method) in which the eosinophiles are estimated in the differential count. The results of the two methods agree.

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COUNTING CHAMBER PEROXIDASE METHOD FOR BLOOD. SIMULTANEOUS RAPID DIFFERENTIAL LEUCOCYTE COUNT AND TOTAL LEUCOCYTE COUNT*

By Akira Sato, and Kenji Shoji, Sendai, Japan

FOR more than two years since the development of the new peroxidase reaction of Sato and Sekiya,[1] we have endeavored to adopt it for use in the counting chamber. The purpose was, first, to shorten the time for routine examination of blood cells and, second, to simplify the technic so that it could be done by a technician without special training. This objective has been attained in the following method.

PROCEDURE

The myeloid leucocytes are stained blue by the peroxidase reaction (copper method) and the lymphocytes red by a counter stain. The sum of these two counts gives the total white count.

Apparatus required: 1. A leucocyte pipette. 2. A counting chamber.

Solution A.—

Aqueous solution of copper sulphate, 1 per cent	90 c.c.
Acetic acid, 30 per cent	1 c.c.
Glycerin	2 c.c.
Distilled water up to	300 c.c.

Filter.

Solution B.—Rub 0.5 gm. of benzidine, pur. Merck (or benzidine base Merck) in a mortar and add distilled water up to 200 c.c. and filter. To the filtrate add 4 drops of 3 per cent hydrogen peroxide. It should be preserved in a brown bottle.

Solution C.—This is a one per cent aqueous solution of safranine. Filter through good filter paper. Before using, pour 2 c.c. of Solution A in a clean watch glass and add two drops of Solution C. Take 2 to 3 c.c. of Solution B in another watch glass.

Draw blood into the pipette up to the 0.3 mark (not 0.5) and after rapidly wiping the end clean, immerse it at once into Solution A plus safranine. Draw up this solution until the mixture fills the lower third or fourth of the bulb of the pipette. Hold a finger over the end and rotate the pipette on its long axis. This causes mixing and avoids the formation of air bubbles. Wait four minutes and then fill to the 11.0 mark with Solution B. Insure thorough mixing by rotation. The fluid is then introduced into the counting chamber.

*From the Department of Pediatrics, Faculty of Medicine, Tohoku Imperial University, Sendai, Japan.

Received for publication, December 2, 1927.

RESULTS

1. Myeloid leucocytes are stained greenish-blue. Monocytes appear faintly red with distinct blue granules.

2. Lymphocytes are stained distinctly red without any shade of blue or green. (Fig. 1.)

REMARKS

1. Differentiation of myeloid and lymphatic leucocytes is easy. All it requires is the ability to distinguish between red and blue. The difference does not depend upon morphologic details, but upon specific biologic relations of the leucocytes.

2. The differential and total cell counts are made simultaneously and require no more time than the usual white count.

3. If by accident some blood is lost or fluid drawn beyond the 11.0 mark or an air bubble is introduced, though the total count is not correct, the differential count is still accurate.

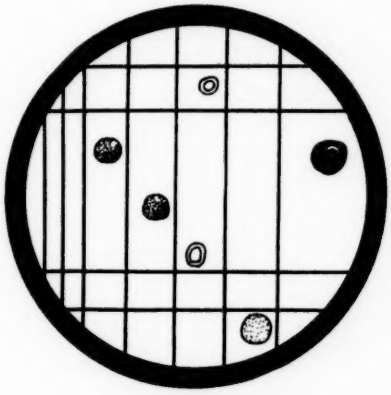

Fig. 1.

PRECAUTIONS

One who tries the present method may wonder why it took so long to develop it after success had been attained with the peroxidase method. Although the technic is simple, one may fail unless certain precautions are taken.

1. It is essential that four minutes elapse after drawing up Solution B plus safranine. We utilize this time in going from the ward (where the blood is drawn and the first solution added) to the laboratory (where the second solution is added and the count made). Any time in excess of four minutes is satisfactory.

2. Fluids should never be withdrawn directly from the bottles, but always from clean watch glasses. Solutions A and B should never be mixed beforehand, nor Solution B and safranine.

3. The mixture in the pipette when filled to the mark 11.0 should appear transparent and light pink, not blue. If both conditions are not fulfilled the stain invariably fails.

4. Blood should not be drawn up higher than 0.3. Beginners fail when they take more, but those with experience never fail even with 0.5. With the smaller amount one never fails to carry all the blood from the capillary to the bulb.

5. Beginners usually draw up too much of Solution A plus C. They should aim to fill the bulb only one-fourth full.

6. Solution A plus C should be drawn up immediately after the introduction of the blood.

7. In mixing, some care must be exercised to prevent the formation of air bubbles. If this has occurred the differential count can still be made.

8. The preesnt method is applicable for human blood only. The treatment of blood of other species will be described in the near future.

9. The microscopic field should show no blue or green fragments. If they are abundant it is a sign of failure.

10. Alcohol and ether should be removed from the cleaned pipette.

11. The low power field should show distinct blue cells. If blue granules can be seen only with the high dry objective, the stain has failed.

12. Solution A keeps indefinitely.

13. Solution B may seem to deteriorate soon, but it keeps for some months in a brown bottle or one year in the dark.

REMARKS

1. After we had succeeded with the peroxidase method given above, we tried the oxidase reaction of Winkler and Schultze[2] with the counting chamber technic and were able to attain success. However, even with freshly prepared reagents, the microscopic field shows much colored detritus. We hope to publish a note on this method soon.

2. The method described has been used in our laboratory for some time. By its use was discovered the first case of agranulocytosis ever reported in Japan.[3] The case was one of apparent sepsis. The field showed no blue (peroxidase-positive) cells.

3. The application of the method to cerebrospinal fluid will be published by Shoji.

SUMMARY

The peroxidase reaction (copper method) of Sato and Sekiya shows a clear differentiation between lymphatic and myeloid leucocytes in the blood smear. The present paper describes the adaptation of that method to the counting chamber.

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A NEW ETHERIZING BOTTLE FOR EXPERIMENTAL WORK*

By D. E. Jackson, Ph.D., M.D., Cincinnati, Ohio

I HAVE experimented with a considerable number of etherizing bottles or devices, but after a year's use, the valve and jar shown in Fig. 1 have been found more satisfactory than any other heretofore used.

The device consists of two parts. Fig. 1 shows the complete device as assembled and ready for use. Fig. 2 shows the metal parts removed from

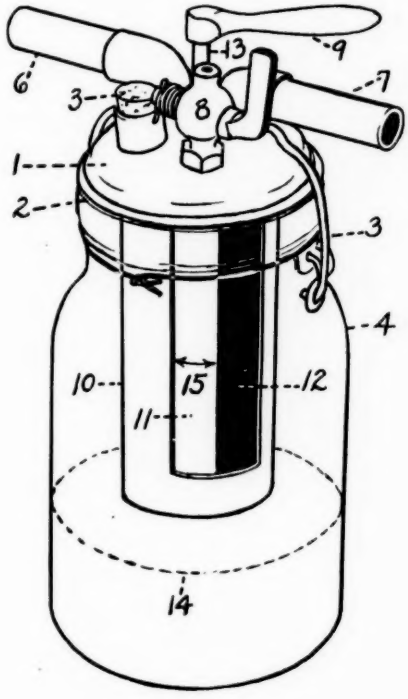

Fig. 1.

the standard, one quart size fruit jar (4) which is filled with ether only up to the dotted circle (14). The breathing tube (6) or (7) is connected to the tracheal cannula by one-half inch size rubber tubing, and the respired air passes back and forth through the tubes and also through the lumen of the double metal, fenestrated cylinders (10 and 11). This inner cylinder (11) is movable and can be rotated inside the outer cylinder (10) by means of the handle (9). There are two large vertical windows in each cylinder. By turning the handle (9) these windows can be rotated around so that the two win-

*From the Department of Pharmacology, University of Cincinnati Medical School, Cincinnati, Ohio.

Received for publication, December 21, 1927.

dows on each side will exactly coincide with each other (thus permitting the ether vapors to pass into the inner cylinder and hence into the respiratory current through the breathing tubes), or the inner cylinder can be turned back so that the outer windows will be partially or wholly closed off by the nonfenestrated parts of the inner cylinder (when only a little or no ether vapor will enter the inner cylinder and the animal will breathe back and forth through the inner cylinder but will get only a little or no ether). By turning the handle back and forth the two double windows can be opened a little (or widely) as indicated by the double arrows at (15). Thus any desired degree of anesthesia can be obtained and in practice a perfectly regular and even anesthesia is easily maintained for hours at a time. The dark space (12) represents the opening into the inner cylinder when the two sets of double windows are about half closed off.

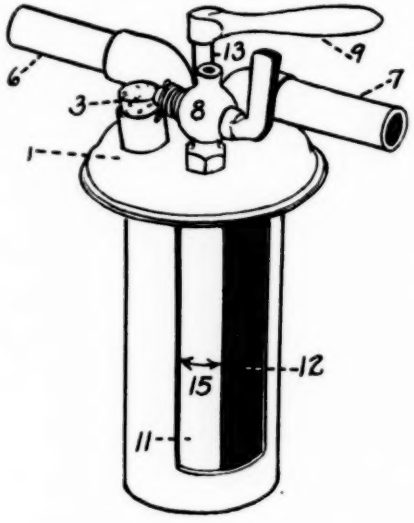

Fig. 2.

The spun metal top (1) carries the breathing tubes (6 and 7) and a tubulature closed by the cork (3). Ether can be poured into the jar through the tubulature while the device is in use. Through the faucet (8) ethyl chloride, carbon dioxide, etc., can be run in through a one-fourth inch rubber tube. The metal top (1) is held on to the jar by the regular wire device (3) which is used to hold on the lid when the jar is used for ordinary purposes. A rubber gasket (2) serves to make the connection air-tight. The rod (13) connects the handle with the inner cylinder.

Artificial respiration can be given through the device without changing any connections or without varying the resistance of the air pressure (and the degree of inflation of the lungs). In fact it was largely to meet this latter requirement that the device was originally designed. For when the chest is open and artificial respiration is being given by means of the usual devices, all the records which are being taken will be disturbed if the amount of ether being given is changed. A T-tube-tracheal cannula should be used and a short

piece of rubber tubing carrying a small screw clamp is placed on the open end of the cannula to secure proper adjustment for the required lung inflation with the given current of air. The device is made by the Max Wocher and Son Co., Cincinnati.

A NEW MYOCARDIOGRAPH*

By D. E. Jackson, Ph.D., M.D., Cincinnati, Ohio

THE myocardiograph here shown was designed especially for dogs but may be used for cats or rabbits. The animal is anesthetized and the chest is opened widely exactly in the midline in the usual fashion. The pericardium is opened longitudinally and each side is attached to the chest wall by one or two stitches so as to hold the heart suspended in a kind of "hammock," but in approximately its regular normal position. The long horizontal arm of the device [i.e., the section between (28) and (31] is brought into position exactly above the opening in the chest, the distance (32) to (31) being directly over the heart and almost in immediate contact. The hinge joint (28) is directed toward the head of the animal and the end of the sternum at the base of the neck must be opened wide enough to permit the section (28) to (26) to move with perfect freedom and without touching any obstruction whatever. This permits absolutely free movement in any direction of the distal part of the horizontal arm where it attaches to the heart.

The apparatus as a whole is grouped on to a base plate (3) which is held fast to a stand (4) by means of the double clamp (1) which firmly holds the supporting rod (2) of the base plate. A horizontal hole is drilled through the base plate and into the right-hand end of this hole the tube (14) is soldered. A small pulley (5) is placed at the lower edge of the left-hand end of the hole drilled through the base plate. The thread (8), which moves the lever (6) passes over the pulley (5) and through tube (14) and tube (16) and over pulley (18) down through tube (20), around pulley (24) through tube (33) and out to the point (32) at which location the thread, *when the device is in use*, is attached to the upper part of the ventricle by one or two small stitches. This attachment is made before the metal bow (30) is sewed to the lower end of the ventricle through a small hole in the metal at point (31).

Thus when the heart beats the contraction of the ventricle will cause a shortening of the distance between the attachment of the thread (32) and the attachment of the metal at (31). The metal arm moves freely in all directions without moving the writing lever but pulling on the thread (which runs over the pulleys) causes immediate movement of the metal writing lever (6).

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Received for publication, December 21, 1927.

Since the horizontal metal arm [(28) to (31)] can move freely without affecting the tracing the respiratory movements of the lungs, etc., will not disturb the record.

The device has hinge joints at (19) and (28). Swivel joints for the tubes are placed at (27), (29), and (17). Longitudinal as well as circular adjustments can also be made at the locking collars (12) and (15) and (21).

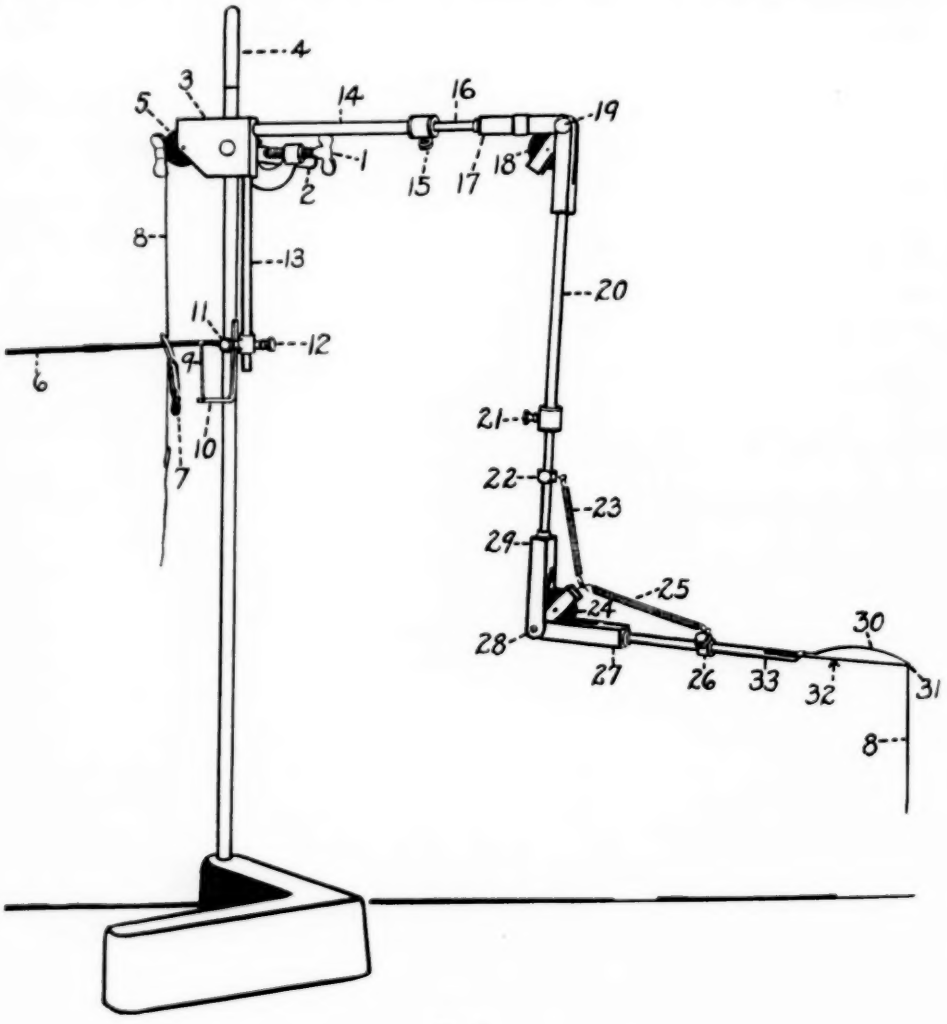

Fig. 1.

The supporting springs (23), (25) are adjusted and held in position by the setscrew-adjusting collars (22) and (26).

Perpendicular and circular adjustments of the writing lever can be made by moving the locking-collar and set screw (12). Tension on the spring (9) is regulated by adjusting the bar (10) which is held by a set screw (11). The thread (8) is best attached to the metal writing lever by a bull-dog clamp (7) which can be adjusted easily and quickly.

I have found this myocardiograph to be sufficiently sensitive and accurate to bring out a number of points about cardiac activity which I had not appreciated before and which I believe no other instrument has shown. The device is made of brass and is nickel plated. It can be obtained from the Max Wocher and Son Company, Cincinnati, Ohio.

STRING SALOL TEST FOR INDICATING PRESENCE OF THE BUCKET IN THE DUODENUM*

By Moses Einhorn, M.D., New York

THOSE physicians who find it necessary to perform frequent biliary drainages are well aware of the lack of a suitable method for indicating that the bucket has entered the duodenum. My experience in this respect has taught me that most of the methods and devices at present in use for this purpose are either impracticable or unreliable. Thus, I have found that the most reliable test is by far the most impractical one. I refer to the practice of fluoroscoping the patient in order to ascertain the presence of the peculiar S-shaped formation of the tube which indicates that the bucket has entered the duodenum. The reliability of this test is, however, offset by its impracticability, for it entails changing the patient's position and this is contrary to the technic of biliary drainage which lays so much stress upon the proper position of the patient. Even were we able to disregard this disadvantage, the fact that so few physicians have fluoroscopes would still prevent this test from being used extensively. Being forced to discard this test because it is impractical, the physician reverts to the usual procedure of using the appearance of bile to indicate that the bucket has entered the duodenum. When this test is employed, we find that although it is to be recommended for its simplicity, we cannot place too much credence in the results it produces because of their uncertainty. This test requires the physician to investigate two possibilities; i.e., the bile may be acid or alkaline in its reaction. If the former, it is bile which has been regurgitated into the stomach; if the latter, it comes from the duodenum. However, the physician cannot always depend upon these reactions to inform him whether the bucket is in the stomach or in the duodenum. It often happens that there remains in the tube sufficient acid from the previous stomach drainage to create an acid reaction in the bile from the duodenum which is passing through the tube. The physician, upon testing the bile and discovering that it has an acid reaction, is often led to believe that the bucket is still in the stomach, whereas, as a matter of fact, it has already entered the duodenum. These few illustrations are sufficient, I believe, to show the need of an apparatus which will eliminate the difficulties described above.

In the course of my work upon the Analytic Bucket,[1] I had occasion to

*Received for publication, December 30, 1927.

make use of the principle often used in pharmacologic preparations when, in order to prevent the preparation from being dissolved in the stomach, a coating of salol (phenyl salicylate) dissolvable only in the alkaline medium of the duodenum is applied to the preparation. It occurred to me that this principle might be used to advantage in solving the problem which confronts us. Accordingly, I have devised the following apparatus which is based upon my New Tip for Gastroduodenal Tubes,[2] the principal characteristics of which are its three-part composition, capsule shape and spiral arrangement. The bottom portion of this Tip was cut off and so modified that it could be connected with the rest of the Tip by means of a screw and thread arrangement. A small piece of brass in the form of a scoop was soldered onto the screw in

Fig. 1.

the severed portion of the Tip in such fashion that it projected within the spiral chamber when the bucket was assembled (see Fig. 1). By means of a thin wire with a hooked end, a length of surgeon's thread is drawn through the tube and attached to the scoop in the following manner: The end of the thread is dipped in phenolphthalein, placed in the scoop and covered with a few drops of melted salol. The salol cools rapidly and upon hardening holds the thread strongly in place. The thread cannot be withdrawn until the salol has been dissolved and, because of the peculiar properties of salol, this can take place only in the duodenum.

This apparatus does not involve any changes in the usual drainage technic.

During the course of the drainage, the physician should tug gently upon the end of the string which emerges from the tube. If the bucket has entered

the duodenum, the action of the alkaline medium will have dissolved the salol and caused the end of the string to turn a scarlet color. The physician then will be able to withdraw the string without disturbing the position of the bucket. If the string cannot be withdrawn, it is an indication that the salol has not come in contact with the alkaline medium of the duodenum and consequently informs the physician that the bucket has not yet entered that organ.

The objection may be raised that this device is not reliable in those cases where there is regurgitation of bile into the stomach, for then, it may be argued, the bile in the stomach will dissolve the salol and permit the string to be withdrawn even though the bucket has not entered the duodenum. This possibility did not escape me when I was experimenting with this device, but as a result of the various tests which I have made, I believe that I can safely say that the objection is not a valid one. In the first place, the amount of bile which is regurgitated into the stomach is usually insufficient to neutralize the acid medium present there. Even were we to grant that regurgitation of bile will create an alkaline medium in the stomach, as for example in those cases of true Achylia Gastrica where there is no acid medium in the stomach, nevertheless, the peculiar properties of salol are such that it is dissolvable only under a steady stream of biliary and pancreatic secretions, particularly the latter, and that is a condition which we can never find in the stomach.

Although I offer this method to my colleagues, confident in the belief that the basic principle is a sound one, I nevertheless realize that there is still room for research and investigation upon several of the minor aspects of the solution which I have advanced. Thus, I have found that it requires much patience and effort to draw the thread through the tube, and since this operation must be repeated before each drainage, I believe that a more efficient method of accomplishing this would add greatly to the usefulness of this device. We must also learn just how thick a coating of salol should be put upon the strips and obtain more information upon the question as to how much time is required for the salol to be dissolved in the alkaline medium of the duodenum.

REFERENCES

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A METHOD FOR READING THE KAHN PRECIPITIN TEST FOR SYPHILIS. THE EFFECT OF CENTRIFUGATION*

By S. L. Leiboff, New York City

OF THE various precipitin tests devised for the diagnosis of syphilis, the Kahn[1] test has met with universal favor. The accuracy of the Kahn test has been fully substantiated by many subsequent investigators. The success of the test rests upon the fact that Kahn recognized the importance of using the ingredients of the test in a highly concentrated form. He adjusted the serum, antigen, and normal saline in proportions that assure the highest degree of concentration possible.

While the Kahn is the most ideal precipitin test for the diagnosis of syphilis, it, nevertheless, has a great drawback in the optical difficulty encountered in reading weakly positive sera, due to the low visibility of the very fine particles that constitute the reaction.

A number of devices have been suggested to overcome this difficulty: Kahn recommends that the reading should be made in front of a partly shaded window against a darkened background, and that in all doubtful tests each tube should be removed from the rack and carefully examined under the most favorable conditions of lighting. Recently, Hopkins and Rockstraw[2] have devised a special illuminating device with the use of artificial standard light to render readings more uniform.

While these devices are helpful, they do not completely eliminate the difficulty, and one has to rely chiefly upon experience and personal equation in reading weakly positive sera. As Kahn[3] recently stated, only especially trained and experienced workers should be considered qualified to perform the test.

In attempting to simplify the reading of weakly positive sera in the Kahn test, it became evident that the difficulty in distinguishing the precipitate in such sera was not due solely to the smallness of the particles, but to other interfering substances. While some sera are particularly cloudy, all of them, even the very clearest, show some degree of opalescence due to the high content of colloidal material. This, together with the highly opalescent antigen, obscures minute precipitates and renders heavier precipitates more difficult of recognition.

We may safely assume that the amount of precipitated substance, particularly in weakly positive sera, is comparatively small in proportion to the rest of colloidal material normally present. Thus, were it possible to remove all extraneous matter, the particles of the precipitate would be far more visible. This can be readily accomplished by means of centrifugation.

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Received for publication, December 12, 1927.

A preliminary trial with a few syphilitic and nonsyphilitic sera was convincing of the practicability of such a procedure. Accordingly this was tested out as follows: Twelve sera were used in the experiment, of which six were positive and six were negative, as shown by the Wassermann test. Of the positive sera four were 4+, one was 2+, and one 1+−. The Kahn test was performed on the twelve sera according to the standard technic. In reading the results no difficulty was encountered with the four 4+, nor with five of the negative sera. Some difficulty was met with the reading of the 2+ serum, but, this was, most likely, due to a very limited experience with the Kahn test. On viewing this serum through a magnifying lens the particles could be seen very easily. With the 1+−, and with one of the negative sera inconclusive results were obtained even with the aid of a lens.

All the tubes were then centrifuged at a moderate speed for five minutes. It then became apparent that all the positive sera, including the 1+− serum, had a moderately large film of opaque material deposited at the bottom of the tubes; the amount of this deposited precipitate apparently being proportionate to the strength of the sera. None of the six negative sera showed a deposited precipitate. The supernatant fluid was then poured off by inverting the tubes. After adding half of one c.c. of saline to each tube, they were shaken vigorously for about half a minute in order to break up the film, and were reexamined. The results obtained are shown in Table I.

None of the tubes containing the negative sera showed particles when examined with the naked eye or with a lens. Most of them appeared almost water clear, while some showed a slight opalescence when viewed against a dark background. This was, doubtless due to traces of material remaining in the tubes, which, of course, is unavoidable. This very faint opalescence, however, could in no way be confused with the precipitated particles in the positive sera.

All the tubes containing the 4+ sera showed great numbers of comparatively large particles suspended in a clear medium. These could easily be seen from a distance of about three feet. The particles in the front tubes appeared somewhat larger and more numerous than in the back tubes. Some of the 4+ sera showed larger particles than others, this being due, most likely, to the varying strength of the different sera.

The 2+ serum showed many particles in the first two tubes. These particles were smaller than any of the 4+ sera, and were fewer in number. The third tube looked doubtful to the naked eye, but through the lens showed distinct minute particles.

The 1+− serum showed very minute particles in the first tube only. The second tube looked doubtful even through the lens, and the third tube was definitely free of particles.

Very definite results were obtained with a hundred more negative and 40 positive sera.

While the number of sera tested is, admittedly, very small, yet, the results are very convincing, and it is hoped that the use of the findings here

set forth as an adjunct to the widely accepted Kahn test, would go far to clear up the discussion as to the relative value of this precipitin test and the Wassermann test in weakly positive sera.

TABLE 1

EFFECT OF CENTRIFUGATION UPON THE PRECIPITATE FORMED IN THE KAHN TEST

SERUM NO.	WASS. TEST	KAHN TEST					
		TUBE 1. (.05 C.C. ANT.)		TUBE 2. (.025 C.C. ANT.)		TUBE 3. (.0125 C.C. ANT.)	
		BEFORE CENTR.	AFTER CENTR.	BEFORE CENTR.	AFTER CENTR.	BEFORE CENTR.	AFTER CENTR.
1	++++	++++	++++	++++	++++	++++	++++
2	++++	++++	++++	++++	++++	++++	++++
3	++++	+++	++++	++++	++++	++++	++++
4	++++	++++	++++	+++	++++	+++	++++
5	++	++	++++	+?	++	−?	+
6	+−	?	++	?	?	?	−
7	−	?	−	?	−	?	−
8	−	−	−	−	−	−	−
9	−	−	−	−	−	−	−
10	−	−	−	−	−	−	−
11	−	−	−	−	−	−	−
12	−	−	−	−	−	−	−

SUMMARY

It was found that the difficulty encountered in reading weakly positive syphilitic sera in the Kahn precipitin test for the diagnosis of syphilis, is not due entirely to the number and size of the particles formed, but to the extraneous substances which obscure the particles. Thus, the reading of weakly positive sera may be made much easier by centrifuging the precipitates, and resuspending them in clear saline.

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DEPARTMENT OF REVIEWS AND ABSTRACTS

ROBERT A. KILDUFFE, M.D., ABSTRACT EDITOR

CLINICAL AND EXPERIMENTAL

IVY POISONING: Observations on the Use of a Modified Extract from Toxicodendron Radicans, Spain, W. C., and Cooke, R. A. Jour. Immunol., xiii, No. 2, 93.

The active principle of poison ivy, Toxicodendron radicans, retains its full potency indefinitely when kept under water-free conditions. This is possible by storing, under calcium chloride, the fresh green leaves, thoroughly dried, or by storing the absolute ethyl alcohol extract of such leaves.

A satisfactory degree of clinical immunity to ivy poisoning can be developed by the administration in proper amounts of the active principle of Toxicodendron radicans, either in the form of oral treatments or hypodermic injections.

The injection method of treatment is preferable, since the conditions surrounding it can be kept more fully under control than in the case of oral administration.

The characteristic lesions of dermatitis venenata can develop upon areas of skin or mucous membrane which have not been in surface contact with the active principle, its transmission to the areas involved being through the blood stream or lymphatics from a distinct focus.

The development of a clinical degree of immunity, as a result of treatment, is indicated by the history of improvement, and not by any demonstrable change upon test in the reaction of the skin toward the active principle.

LABORATORY TECHNIC

CULTURE MEDIUM: A Modification of the Kligler Lead Acetate Medium, Bailey, S. F., and Lacy, G. R. Jour. Bacteriol., 1927, xiii, No. 3, 183.

The essential points noted are:

1. Phenol red gives more satisfactory results as an indicator than Andrade's indicator which is used in the Kligler medium.

2. It is not necessary to add the sterile lead acetate to melted sterile agar tubes, but all of the ingredients of the medium can be mixed in bulk at a temperature of 50° C. or lower thus preventing flocculation. The lead acetate can be added either in crystals or in solution. The medium can then be tubed and sterilized by heating in the autoclave at 5 pounds pressure for twenty minutes.

3. No damage occurs and no flocculation takes place, even though sterilization be accomplished by heating at 15 pounds pressure for fifteen minutes.

4. The browning of the lead acetate medium is due to the formation of lead sulphide and in the absence of this medium, the production of H_2S by organisms may be determined by suspending in the neck of the culture tubes strips of white filter paper saturated with lead acetate solution.

5. The preparation of the medium thus simplified makes it thoroughly practical for use in teaching laboratories and in public health diagnostic laboratories.

To each 100 c.c. are added 1 gm. of lactose, 0.1 gm. of glucose, 0.05 gm. lead acetate, and 5 c.c. of 0.02 per cent aqueous phenol red, the medium having first been cooled to 50° C.

The following formula was used throughout as a basis for the medium:

Bacto-beef extract	5 grams.
Pepton (P. D.)	10 grams.
Sodium chloride (B. & A.)	5 grams.
Agar shreds	15 grams.
Tap water	1000 c.c.

The agar was first thoroughly washed in running water and was then heated in the required amount of water, until it was dissolved, after which the other ingredients were added. The reaction was adjusted to P_H 7.4 and the medium was boiled for from five to eight minutes. At the end of the heating, the reaction was readjusted to P_H 7.4 and the sediment allowed to settle to the bottom of the container. The clear supernatant agar was then decanted into another container and was accurately divided into quantities of 100 c.c. and sterilized by heating at 10 pounds pressure for twenty minutes.

PREGNANCY: Postmortem Findings in Ten cases of Toxemia of Pregnancy, Bell, J. W. Am. Jour. Obst. and Gynec., 1926, xii, No. 6, 792.

In these cases there is little agreement in the liver lesions, which include passive congestion, localized fatty infiltration, acute yellow atrophy, infarction, hemorrhagic necrosis, cellular infiltration (chiefly of portal spaces). These data weaken our belief in any one lesion of the liver being considered essential for toxemia of pregnancy.

RABIES: A New Stain for Negri Bodies, Sellers, T. F. Am. Jour. Pub. Health, 1927, xvii, 1080.

Basic fuchsin (saturated absolute methyl alcohol solution)	2-4 c.c.
Methylene blue (saturated absolute methyl alcohol solution)	15 c.c.
Methyl alcohol (absolute acetone free)	25 c.c.

The methylene blue and the methyl alcohol are mixed in a Coplin jar and 2 c.c. of the saturated fuchsin solution is added. A trial stain is made. Macroscopically the properly stained smear, when held up to the light, should appear reddish violet in the thinner areas shading into purplish blue in the thicker portions. If in the trial stain the thinner parts are bluish, 0.5 c.c. more fuchsin should be added and another trial made. Two c.c. of fuchsin solution is nearly always sufficient. The mixed stain seems to improve after twenty-four hours' standing and thereafter keeps indefinitely if protected from evaporation, which tends to make the fuchsin become too dominant. The addition of absolute methyl alcohol to the evaporated stain will usually restore the proper balance to the two dyes. On the basis of the above formula the stain may be prepared in any quantity, and if kept tightly corked will maintain its quality indefinitely.

TECHNIC OF STAINING

Thin smears from the Ammon's horn hippocampus are prepared in the usual way and while still moist with tissue juice are plunged into the stain, removed immediately and rinsed under the tap. The entire process should be completed in less than five seconds. The stained slide may be dried by warming and waving through the air. Blotting is not recommended because the wet smear is very easily wiped from the glass.

The low power two-thirds objective should first be used in examining the stained smear. Thin areas showing numerous large nerve cells well spread out should be spotted and then examined with the oil immersion.

CARCINOMA, "MALIGNANCY INDEX" IN: The Significance of the Histological "Malignancy Index" for Prognosis and Treatment of Carcinomata of the Cervix Uteri, Schmitz, H., Hueper, W. and Arnold, L. Am. Jour. Roentgen. and Radium Therapy, July, 1926, xvi, 1, 30.

In this paper, illustrated with 12 microphotographs, the authors describe their method of determining the "malignancy index."

The following factors were used:

1. Special cell type of carcinoma. Each of the four sub-groups of carcinomas were used as a basis in this special cell type classification. The cornified spinous cell carcinoma was given a value of 2; uncornified spinous cell carcinoma a value of 4; round cell car-

cinoma a value of 6; and the spindle cell carcinoma a value of 8. The same general scheme was carried through with the glandular carcinomas. The maturity of the majority of cells present was the main factor used to determine this grouping. The more embryonal and anaplastic the component cells, the greater is the proliferative power and the higher the potential malignancy.

2 and 3. Irregularities in size and shape of the cells. The average shape or size was studied. If 50 per cent of cells showed irregularity in size and shape then the value 4 was given; if 30 to 40 per cent, the value 3; if 20 to 30 per cent, the value 2; and if 10 to 20 per cent, the value 1.

4. Distinctness in outline of the cells. The cells with distinct and sharp outline were evaluated as 1. If 50 per cent were indefinite in outline the value 2 was given; if 75 per cent, the value 3; and if more than 75 per cent had an indefinite outline a value of 4 was given.

5. Functional activity of cells. This was estimated from the presence in the cells of keratin granules, mucus, etc. If the majority of the cells showed a functional activity, the value 1 was given. Minor degrees were evaluated as 2, 3, and 4 respectively. The same relative percentages were used as in the previous standards.

6 and 7. Irregularities in the size and shape of the nuclei of the cells. The size and shape shown by the majority of the nuclei present were taken as the standard size and shape. A deviation of 50 per cent from this standard was evaluated 4; a deviation of 30 to 40 per cent 3; of 20 to 30 per cent as 2; and less than 20 per cent as 1.

8. Staining quality of the nuclei. Cells containing nuclei taking the stain as intensely as the nuclei of lymphocytes were considered hyperchromatic. When 25 per cent of such hyperchromatic nuclei were present, the value of 4 was given; 20 to 25 per cent a value of 3; 10 to 20 per cent a value of 2; and 5 to 10 per cent a value of 1.

9. Number of mitoses and prophases. These two were counted separately but considered together as indicative of proliferative properties. Ten fields were counted with oil immersion lens (1050 x magnification) giving an actual count on the mitotic figures on which to base an estimate of proliferative activities of the carcinoma examined. In case 20 or more mitotic figures were seen in the 10 fields, a value of 4 was given; 15 to 20 mitoses were evaluated as 3; 10 to 15 as 2; and below 10 as 1.

An examination of the tables in the paper will show how the numerical values of the various factors are put in a certain system which was named "malignogram" (Hueper) and when added together give a number to which the term "histological malignancy index" (Hueper) was applied.

In addition to these, it is suggested that a study of the factors below would increase the value of the "malignogram."

1. Special type of carcinoma.
2. General type of the carcinoma.
3. Absolute size of the cells.
4. Irregularities in size of the cells.
5. Absolute shape of the cells.
6. Irregularities in shape of the cells.
7. Distinctness in outlines of the cells.
8. Staining quality of the cells.
9. Functional activity of the cells.
10. Absolute size of the neuclei.
11. Irregularities in size of the nuclei.
12. Absolute shape of the nuclei.
13. Irregularities in shape of the nuclei.
14. Absolute staining quality of the nuclei.
15. Irregularities in the staining quality of the nuclei.
16. Number of mitoses and prophases.
17. Irregularities in form of the mitoses.
18. Character of the stroma.

19. Vascularity of the stroma.
20. Degree of round cell infiltration.
21. Character of round cell infiltration.

From such a study four groups may be made:

Group 1 showed an average Malignancy Index of 21.0.
Group 2 showed an average Malignancy Index of 23.11.
Group 3 showed an average Malignancy Index of 23.07.
Group 4 showed an average Malignancy Index of 22.81.

The paper may thus be summarized:

1. The cell types, the differentiation, and the anaplastic changes of carcinomas of the cervix have been studied. They were given a numerical value, the sum representing the histologic malignancy index.

2. Immaturity of the cells, a low degree of differentiation and a high degree of anaplastic changes are invariably associated with a high malignancy index.

3. The greater the maturity of the cells, the higher the differentiation and the less the anaplastic changes are, the lower will be the malignancy index.

4. The clinical malignancy of a carcinoma depends solely on the results of treatment obtained, provided the same method of treatment was used in each case. The extent of the carcinoma influences the outcome then only if it has thereby become a systemic or generalized disease (Group 4 cases). A carcinoma contained within a well-defined area and having a low malignancy index offers every hope for a relatively good prognosis.

5. Comparing the histologic malignancy index with the clinical findings or grouping of the carcinomas and excepting the Group 4 cases, it is found that a definite relation between the two does not exist.

6. The relation of the cell type to the histologic malignancy index is definite. The unripe cell type is almost always associated with a high malignancy index.

7. The relation of cell type to the clinical result is not as definite as the relation of the malignancy index to the clinical result. The malignancy index shows a definite or proportionate relation to the result of treatment obtained.

8. Considering the relation of the malignancy index to the clinical result and excluding the Group 4 cases, we may conclude that the pathologist can give definite information as to the degree of malignancy from a histologic examination expressed in numbers of the malignancy index, which will enable the clinician to choose those cases of carcinomas which may respond with fair prospects to radiation treatment.

AGGLUTINATION TESTS: A Simple Reaction for Detecting the Binding of Agglutinins by Difficultly Agglutinable Suspensions, Mudd, S. Jour. Immunol., 1927, xiii, 2, 113.

The resuspension reaction consists essentially in centrifugalizing the bacteria after exposure to serum and then resuspending the sediment by shaking. The intensity of the reaction is given by the size of the resulting clumps.

The bacterial suspension and serum dilutions are prepared, mixed, allowed to stand, and the macroscopic agglutination readings are made in the usual way. All tubes are then centrifuged until clear; the salt solution controls are usually the last to clear and serve to indicate when centrifugalization may be stopped. The tubes are then arranged serially in a rack with the controls and several of the highest serum dilutions in the middle. The rack is held with one hand at each end and shaken with an even backward and forward motion so as to make agitation of all tubes as nearly equal as possible. The control tubes are watched carefully during the agitation and as soon as their sediment has again become evenly suspended shaking is stopped. The tubes containing well sensitized bacteria still show flocculi increasing in size to the highest serum concentrations. Many of these clumps may break up if agitation is too prolonged, however, too low an apparent titer resulting.

After the results of the first resuspension are recorded it is often advantageous to make a check test. The tubes are accordingly again centrifuged until clear. The supernatant

fluid may be decanted by a quick inversion of the tubes without serious loss of sediment. Two drops of isotonic NaCl solution are then added to each tube; they are arranged in a rack and shaken as before, but more gently, until the control tubes become even. Flocculi are again recorded. The results of the two resuspension tests are usually in essential accord, and either one will often be sufficient by itself.

It is important that the internal diameter of all the test tubes used in this test, and the volume of liquid in each be approximately the same. A given amount of agitation will ordinarily break up the clumps less in narrow than in slightly wider tubes and less with large than with smaller volumes of liquid.

COLORIMETRY: A Simple Colorimetric Method for the Determination of Iodine in the Urine, Yoshimatsu, S., and Sakurado, H. Tohoku Jour. Exper. Med., 1926, viii, 4, 107.

The method depends upon the reduction of silver iodide previously dissolved in potassium cyanide solution, and the production of a dark brown color, which is applied to colorimetry. The reduction is effected by sodium sulphide.

Solutions required:

1. Standard silver nitrate solution A. Dissolve 1.338 gm. of silver nitrate in distilled water and make up to 100 c.c. 25 c.c. of this solution is made up to 500 c.c. with distilled water. 10 c.c. of this solution equals 0.005 gm. of iodine.

2. Standard silver nitrate solution B. 2.907 gm. of silver nitrate is dissolved in distilled water and made up to 100 c.c. 25 c.c. of this solution is made up to 500 c.c. with distilled water. 10 c.c. of this solution equals 0.005 gm. of sodium chloride or 3.04 mg. of chlorine.

3. Nitric acid (5N).

4. Concentrated silver nitrate solution. Silver nitrate 50 gm. aqua destillata ad 100 c.c.

5. Aqua ammoniae (10 per cent).

6. Potassium cyanide (5 per cent).

7. Gelatine solution (10 per cent). Ampoules for injection may be used with satisfaction.

8. Fuming nitric acid.

9. Chloroform.

10. Potassium iodide solution (1.3 per cent).

11. Sodium sulphide (10 per cent).

METHOD

Determination of amount of urine to be used for analysis.

Rinse 0.05 c.c. (0.5 mg. of iodine) of 1.3 per cent potassium iodine solution into a 25 c.c. calibrated test-tube. Put 0.5 c.c. of urine in another test tube of the same kind. Add to each tube 2.5 c.c. of distilled water and 3 drops of fuming nitric acid. Make up to about 10 c.c. with chloroform. Then mix and compare the colors. If the urine tube is much lighter, add another 0.5 c.c. of urine again and again, until an approximate intensity of color is reached. Then the whole amount used for the test is one tenth the amount to be used for the quantitative determination by the present method.

Method of analysis.—Measure an optimum amount of urine for one sample as described above. Then pipette a certain amount (usually 1 c.c. is sufficient) from this measured quantity into a centrifuge tube of 25 c.c. contents (chloride tube) for the determination of chlorine. Divide the rest of the sample together with rinsings of the pipette (as little water as possible should be used for rinsing) in two or four centrifuge tubes of the same contents. Add to each tube the same amount of water and 1 c.c. of nitric acid (3), and then 2 c.c. of concentrated silver nitrate solution (4). Stir and centrifuge until the supernatant fluid becomes clear and remains so on a further addition of drops of silver nitrate solution. Pour off the supernatant fluid and wash the precipitates with distilled water three times. Add 1 c.c. of aqua ammoniae (5) to the chloride tube above mentioned and about half an amount

of the same corresponding to the urine quantity to all the other tubes. Stir well and centrifuge again. Transfer the supernatant fluid of the chloride tube into a 100 c.c. volumetric flask and make up to about 80 c.c. with distilled water. Put 10 c.c. of standard silver nitrate solution B (2) into another 100 c.c. volumetric flask and pour in 2 c.c. of aqua ammoniae and 50 c.c. of water. Add 1 c.c. of gelatine solution (7) and 2 c.c. of sodium sulphide (11) to each flask. Wait one minute and fill up to mark with water. Compare the colors thus developed in a Duboscq colorimeter by setting the standard at 20.0 mm. The calculation is as follows:

$$\frac{\text{Reading of standard}}{\text{Reading of unknown}} \times 0.005 \text{ gm.} = \text{NaCl or } 3.04 \text{ mg.} = \text{Cl in amount of urine taken.}$$

As to the other tubes (iodine tubes) pour off the supernatant fluid and wash the precipitates three times. Add 1 c.c. of potassium cyanide solution (6) to each tube and dissolve the precipitates. Transfer the contents of all the tubes into one and the same 50 c.c. volumetric flask. Put into another 50 c.c. volumetric flask exactly 10 c.c. of standard silver nitrate solution A (1) and add 1 c.c. of potassium cyanide solution (6). Then add 0.5 c.c. of gelatine solution (7) and 2 c.c. of sodium sulphide (11) to each flask. A brown color develops immediately. Wait one minute and fill each flask up to mark with water. Compare the colors in a Duboscq colorimeter, setting the standard at 20.0 mm. The calculation is as follows:

$$\frac{\text{Reading of standard}}{\text{Reading of unknown}} \times 0.005 \text{ gm.} = \text{I in amount of urine taken.}$$

AGGLUTINATION: A Rapid Method for the Macroscopic Agglutination Test, Noble, A. Jour. Bacteriol., 1927, 14, 5, 287.

The test is made in small test tubes (75 x 13 mm.).

Place 0.1 c.c. of heavy bacterial suspension in a tube and add 0.1 c.c. of the serum diluted 1:10 with N/8. In another tube (control) place 0.1 c.c. of bacterial suspension and 0.1 c.c. of N/8.

Place the tubes in a rack and, inclining the rack so that the mixture flows up the tube about one inch, shake for two minutes. Then add 0.8 c.c. N/8 to each tube and read for agglutination.

The serum dilution cited is 1:100. Dilutions may be made in series as desired.

REVIEWS

Books for Review should be sent to Dr. Warren T. Vaughan, Medical Arts Building, Richmond, Va.

*Neuberger's History of Medicine**

THIS section of Neuberger's monumental history deals with medicine in the Middle Ages. The entire work is not yet available in English but the publishers are to be congratulated on going ahead with the publication of that section which is now available.

So many of the medical histories pass over the Middle Ages with scant attention because so little of real progress was contributed in this Dark Age in medicine. If one will but stop to consider, however, one must realize that there must have been events during these times many of which are of decided historic interest, even though they do not mark steps of great progress in our knowledge of the arts and sciences.

The story of the school of Salerno in its prime and during its decadence is alone an hour of enjoyable reading. The Arabic influence upon western medicine, known to all, is more readily understood after reading Neuberger. We usually understand that the writings of Hippocrates were preserved for us in the Arabic until the Renaissance. But when we understand how they were translated from the Arabic, we are in a better position to understand how fragmentary, incomplete, and erroneous our present knowledge of the Hippocratic writings is. The Italian translator, having little or no familiarity with Arabic, caused the text to be read to him in the Spanish vernacular by some one well acquainted with the language and wrote it down at once in Latin from this dictation. The slavish translation word for word makes it readily comprehensible that grotesque perversions of meaning are not uncommon. Frequently it appears as though the reader was left by the unintelligent translator to read his own meaning into the confused text.

We are inclined to think of the early Church as having stifled medicine. In a sense this is true, but at the same time it was the church and the church alone that in its monasteries maintained what few traditions were carried on through the Dark Ages.

Neuberger's volume accomplishes one feat which is too often lacking in medical histories, it gives the reader a sensation of actual personal acquaintanceship with the actors as they pass on and off the stage.

The Specialties in General Practice†

THIS work deals with those more common diseases which by reason of their location are usually treated by the specialists but which could probably be treated as satisfactorily by the family physician, provided he knew the most acceptable treatment to be applied and were willing to apply it. Those diseases whose treatment requires special skill or the use of unusual instruments are not detailed.

One may pick up the volume in a search for information concerning the treatment of a special disease. But it is pleasant reading, and one will read on only to find later to his

*History of Medicine. By Dr. Max Neuberger, Professor of Medical History in The University of Vienna. Translated by Ernest Playfair, M.B., M.R.C.P. In Two Volumes, Vol. II Part I. Paper. Pp. 135. Oxford University Press, American Branch, N. Y.

†The Specialties in General Practice. Compiled by Francis W. Palfrey, M.D., Instructor in Medicine at Harvard University in Collaboration with The Author's Names on Page 9 in Their Respective Subjects. Cloth. Pp. 748. W. B. Saunders Company, Philadelphia, Pa. 1927.

NOTE: In so far as practicable the book review section will present to the reader (a) interesting knowledge on the subject under discussion, culled from the volume reviewed, and (b) description of the contents so that the reader may judge as to his personal need for the volume.

We trust that the scientific information printed in these pages will make the reading thereof desirable per se and will thereby justify the space allotted thereto.

surprise that he has quite unconsciously covered quite a large portion of the book and at the same time quite a wide range of medicine. One finds no revolutionary in the therapeutic outlines and gains the impression that the work is based on didactic lectures to senior medical students. But at the same time the reader is surprised to discover how refreshing it is to renew acquaintance with old friends and on every page or two pick up a valuable tip either new or forgotten which he will undoubtedly have an opportunity to apply in his work in the not far distant future.

We might characterize the volume briefly "An Excellent Post Graduate Course" for the general practitioner. Those diseases which rightly fall within the domain of internal medicine are not discussed within the volume. In those conditions which are discussed, diagnosis is touched upon but treatment in particular is emphasized.

*Physical Diagnosis of Diseases of the Chest**

HERE is a new method of attack and treatment. One hundred pages devoted to fundamental considerations, such as, methods of examination, the physics of sound, and the technic of examination. Twenty odd on the examination of the healthy chest. All of this before there appears any discussion of the lungs in disease, and this latter section is no longer than the first. To one who is impatient to get to the end of a book or to get down to the so-called practical aspects this will be a bit tedious. But to one for whom a thorough grounding and understanding of his subject is the first consideration, the volume should be most alluring.

Dr. Bushnell devotes considerable space to the tuberculous chest with the remark that after one has mastered the diagnosis of pulmonary tuberculosis in its various forms, the diagnosis of other diseases of the lungs is found to be relatively easy. His wide army experience with early and incipient tuberculosis makes Dr. Bushnell an authority on the subject.

Dr. Pratt's discussion of the diagnosis of diseases of the heart follows more closely the conventional lines, but his presentation is built upon a wide experience, and a clear insight which makes his work easy reading and should enable one to apply the principles enunciated with distinct success. The illustrations are abundant and excellent. Dr. Pratt, like the late Sir James Mackenzie, emphasizes that the true cardiologist is the man, who when the occasion arises, can successfully dispense with the various instruments which have been devised for cardiac study.

Symptom Diagnosis†

THE author outlines three outstanding purposes of the volume; first, to aid the busy physician in the diagnosis of his case by allowing him to quickly reduce the number of possibilities to a small list; second, to prevent the oversight of important considerations; and third, to make the medical man more observant of the characteristics of the symptoms of disease. It is purely a reference manual and as such is excellently arranged. The examiner can find in a few minutes the various causes both common and uncommon of the patient's chief complaint. Bearing these in mind he may then execute his physical examination, searching for evidence of one or another of these causes. A definite tendency in the examination of the patients is to suspect a particular malady after having heard the patient's story and, therefore to carry out the examination with the perhaps unconscious intention of confirming this suspicion. This is probably one of the most frequent causes for error in diagnoses. Suspended judgment throughout the examination is essential but its value is surely enhanced if at the same time one is intelligently on the *qui vive* for all

*Physical Diagnosis of Diseases of the Chest. By Joseph H. Pratt, A.M., M.D., and George E. Bushness, Ph.D., M.D. With 166 Illustrations. Cloth. Pp. 522. W. B. Saunders Company, Philadelphia. 1925.

†Symptom Diagnosis. Regional and General. By Wilfred M. Barton, A.M., M.D., F.A.C.P., and Wallace M. Yater, A.B., M.D. Cloth. Pp. 851. D. Appleton & Co., New York. 1927.

possibilities. For the purposes for which it was prepared this volume may be highly recommended. The outlines are brief, concise and to the point and with the help of the table of contents and index the different symptoms are found most readily.

The authors are to be felicitated on a happy selection in dedicating the volume to Dr. George M. Kober, venerable dean among Washington's physicians, a man of delightful personality, a guiding spirit of Georgetown University.

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*Diet and Dietetics**

A COMPILATION by various British authors most of whose names are well known on this side of the Atlantic. As the editor remarks in his preface, until our knowledge of physiology is more perfect than at present, the scientific basis of dietetics must be an unstable one. Nevertheless, patients must be dieted and the physician must be guided by the teachings of history, by experimental physiology, and by clinical experience in the proper regulation of the diet.

Sir Lauder Brunton opens the discussion with an introduction on the general principles of dietetics. Next follows a chapter by Harry Campbell on the evolution of man's diet in which he brings out the noteworthy fact that man has advanced to his present state on a diet which is in great part carnivorous. One may, therefore, rightly question the claims of the vegetarian that flesh is not appropriate to man.

Dr. E. I. Spriggs describes the physiology of digestion, absorption and nutrition and devotes many pages to the diet in health. Edmund Cautley tells us that proprietary foods are not necessary either in sickness or in health. The greater the knowledge possessed by the individual of the composition of natural and proprietary foods and of the various means of modification by simple home methods, the less will he find it necessary to have recourse to the manufactured article, and the better will be the results of his dietetic treatment. Although unnecessary, it must nevertheless be clearly realized that such foods are sometimes of greatest value. It is equally important to realize that a knowledge of the composition is essential to the proper utilitization of any proprietary food. The composition of a great variety of proprietary foods is described in detail.

Dr. Harry Campbell's chapter on alcohol is especially readable. Alcohol has been known to man probably for about thirty thousand years, coming into existence with the development of agriculture. Only for fifteen thousand years has it been used more or less to excess, because prior to that time there were not facilities for storage. Dr. Campbell does not make out a good story for alcohol either in health or disease. Alcohol leads to the production of heat which, however, is met by a corresponding or even greater heat loss. It may furnish energy but it diminishes the capacity for sustained muscular work. It promotes the laying on of fat and diminishes the amount of food needful to sustain body weight. Even the moderate drinker has a poorer life expectancy than has the total abstainer.

Dr. Campbell finds a better remedy than alcohol in nearly all of those diseases in which alcohol may be prescribed. Occasionally it may be of distinct value, however, in acute cardiac emergencies or in fatal diseases such as sarcoma or advanced phthisis.

The appropriate diets in various diseases are contributed by different authors. Many of the "cures" used at health resorts on the continent and in England are described. This should give the volume value as a reference work in America.

The discussion of diabetes is too brief.

The presentation of diets for individual diseases follows the usual routine and is open to the usual criticism. Too much attention is paid to those diseases in which diet is of minor importance and too little to those fewer diseases in which diet is a major consideration. The section on diet in infancy and childhood is good. So also is the short chapter on diet in old age.

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*A System of Diet and Dietetics. Edited by G. A. Sutherland, M.D., F.R.C.P. Second Edition. Cloth. Pp. 893. Physicians and Surgeons Book Company, New York.

*Histology of the Endocrine Organs**

TEXTBOOKS on histology describe in detail the microscopic picture of the various organs of internal secretion. But with few exceptions account is not taken of the age factor, and yet as one will see at a glance age may play a distinct part in altering the histologic picture of this type of tissue. Dr. Cooper has made careful comparative studies of the thyroid, parathyroid, pituitary, suprarenal, and thymus glands at different ages. All the work was with human material. The author observed decided differences in different age periods. She did not make a study of the sex glands.

Diseases of the Skin†

A RICHLY illustrated textbook on dermatology, of encyclopedic proportions. Most physicians and too many pseudodermatologists know far too little of the great variety of afflictions to which the skin is heir. So many cutaneous manifestations respond readily to a few drugs such as sulphur, mercury, zinc oxide, tar, or arsenic internally, that the usual procedure is, we venture to say, the mumbling offhand of an indistinct or nondeterminative diagnosis and the prescribing of some old favorite ointment. The condition failing to respond, the physician scratching his head, makes some remark about an unusually refractive case, and the patient continues with his disease. In scarcely any domain of medicine is it so true in dermatology, that, the correct diagnosis having been arrived at, the indications are clear cut and are specific for each condition. And in diseases of the skin where all or nearly all of the pathologic alterations are so accessible for study, in justice to his own self-respect, the physician should not be content without the most thorough and painstaking diagnostic scrutiny.

A volume such as Sutton's in which the illustrations are so clear and abundant and in which the text is thoroughly descriptive will serve as an excellent reference manual.

To those working to keep abreast of the more recent therapeutic advancements in dermatology, the reviewer would recommend particularly the chapters in the Parasitic Skin Infections, especially the mycotic disorders.

Textbook of Pathology‡

A TEXTBOOK of general and special pathology reflecting particularly the concepts in pathology as developed in the University of Edinburgh. The text is clearly written, the headings and the points for emphasis are easily followed, being printed in boldface type and the work is most profusely illustrated with excellent photographs, colored plates, and photomicrographs.

The interest throughout the work is preeminently in structural pathology, there being practically no discussion of clinical pathology, although a brief chapter is devoted to immunity.

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*The Histology of the More Important Human Endocrine Organs at Various Ages. By Eugenia R. A. Cooper, M.D., Demonstrator of Anatomy and Late Leech Fellow of the Victoria University of Manchester. Cloth. Pp. 119. Illustrated. Oxford University Press. American Branch, New York.

†Diseases of the Skin. By Richard L. Sutton, M.D., LL.D., F.R.S. (Edin.) Professor of Diseases of the Skin, University of Kansas School of Medicine; Assistant Surgeon, U. S. Navy, Retired; Member of the American Dermatological Association; Dermatologist to the Atchison, Topeka and Santa Fe Hospital Association; Dermatologist to the Christian Church Hospital. 1237 illustrations and 11 colored plates. Seventh Edition Revised and Enlarged. Cloth. Pp. 1694. The C. V. Mosby Co., St. Louis, Mo.

‡A Textbook of Pathology, General and Special, for the use of Students and Practitioners. By J. Martin Beattie, M.A. (N.Z.), M.D. (Edin.), M.R.C.S., L.R.C.P. (Lond.) and W. E. Carnegie Dickson, M.D., B.Sc., F.R.C.P. (Edin.) Cloth. Illustrated. Pp. 1103. C. V. Mosby, St. Louis. 1926

*Electrothermic Methods in Neoplastic Diseases**

A HANDBOOK on diathermy, electrodesiccation and electrocoagulation. The author presents a brief description of electricity, types of electrical current, chemical and physical effects of these currents, their use in medicine and surgery, and the instruments best suited for this manipulation.

A large portion of the book is devoted to the action of electrodesiccation and electrocoagulation in specified conditions. The author does not limit himself to neoplastic diseases but describes the results of this treatment also in such conditions as fissure, fistula, hemorrhoids, corneal ulcer, chanceroid, x-ray dermatitis, tattoo marks, tonsil removal, and chronic ulcers.

The last chapter consists of a series of practical laboratory exercises in the use of the machines, using the operator himself, meat, potatoes, soap, etc., as subjects.

The Abdomen in Labor†

THE author takes exception to the custom, apparently altogether too prevalent in England, of making routine vaginal examinations of the parturient woman. The obstetrician is inclined to concentrate his attention on the uterine cervix, a part which he cannot see, and with his eyes at his finger tips, attempts to gain the information he thinks he requires, from the insignificant fraction of the uterus projecting into the vagina. But the cervix and os uteri play not an active part but a passive part in labor. The changes forced upon the inert cervix are entirely the result of the action of the great body of muscle above it. It is not in the cervix but in the powerful, contracting, muscular mass of the uterus that the essential phenomena of labor occur.

The author concludes after years of study of the abdomen during labor that a wealth of valuable and instructive information is usually lost to the obstetrician because of his failure to inspect the abdomen and to gain that knowledge which is made available to palpation. By inspection of the abdomen he implies, of course, a really intelligent study of the contors and prominences at various stages particularly when the patient is in pain and not in pain. Dr. Porritt feels that as a rule the position and presentation and the presence of most abnormal conditions, except those directly at the cervix, can be as readily identified by abdominal examination as by vaginal examination and with far less risk to the patient.

His description of the findings within the abdomen during labor is illustrated with drawings made at the bedside.

Old and New Viewpoints in Psychology‡

AN AUTHORITATIVE, critical discussion of certain phases of psychology which have caught the popular fancy and have been adopted by pseudoscientists usually for personal gain. This includes particularly Freudian psychoanalysis, intelligence tests, spiritualism, and character analysis. There is also a delightful chapter on the psychology of the comic.

The author has no objection to intelligent tests as one form of mental measurement when properly applied. The trouble is that in the past it has been too frequently misapplied. The Binet-Simon tests were developed as a means of measuring the intelligence of children, and their evolution covered a number of years in which painstaking study was made. At the onset of the war an attempt was made to develop similar tests for

*Electrothermic Methods in Neoplastic Diseases. By J. Douglas Morgan, B.A., M.D. Electrothermic Methods or (Desiccation and Coagulation in the Treatment of Neoplastic Diseases. Designed as a Practical Handbook of Surgical Electrotherapy for the use of Practitioners and Students. By J. Douglas Morgan, B.A., M.D. Cloth. Illustrated. Pp. 172. F. A. Davis Company, Philadelphia.

†The Abdomen in Labor. Being a General Practitioner's Clinical Study of the Parturient Abdomen. By Norman Porritt, M.R.C.S., L.R.C.P. (Lond.), Consulting Surgeon, Huddersfield Royal Infirmary. Cloth. Pp. 76. New York, Oxford University Press, 1926.

‡Old and New Viewpoints in Psychology. By Knight Dunlap, Professor of Experimental Psychology in the Johns Hopkins University. Cloth. Pp. 166. The C. V. Mosby Company, St. Louis, Mo. 1925.

recruits, many of which were unscientific, and therefore, unsuccessful. Thus the testing of an aviator for his reaction to various stimuli told nothing. But the more recent tests which measured his ability to manage a complicated series of reactions analogous to the operations and discriminations required of him in his airplane told a great deal.

The Binet-Simon test is not simply a language test. A moron may have considerable fluency in language, but he does not pass the Binet-Simon test. This test measures acquisition almost exclusively. From the measure of what knowledge the individual has actually acquired we estimate his future capacity to acquire. The individual is a moving body and by plotting the course he has passed over we predict future developments.

The application of even the best intelligent tests requires intelligence. A school teacher or a nurse or even a physician cannot read over the principles of the test and then apply them correctly. The matter of interpretation requires experience. Too frequently inexpert testers have rated feebleminded children as normal and normal or even exceptionally bright children as feebleminded.

The statement has been made that the average mental age of the draft was 13.5 years. This is viciously misleading, for the Binet-Simon scale of ages stops at fourteen, the following two grades being adult and superior adult. These latter are sometimes specified as sixteen and eighteen years respectively. It is readily seen, therefore, that an averaging of mental ages, not taking this into account, will explain the erroneous impression given.

Dr. Dunlap believes in intelligence tests properly applied. This means a special set of tests for each individual problem. One set for switchboard operators, another for telegraphers, another for jobs in rubber factories, etc.

The author has scant patience for the Freudian psychology and psychoanalysis which he discusses at some length. There is no basis in experimental psychology for the so-called subconscious mind. "Nothing could be more vicious or absurd than the doctrine of repression. Actual repression is the only salvation of man if civilization is to continue, and the ability to repress effectively is the greatest asset a human individual can have." "Nothing is more weakening than to keep thinking of past mistakes and illicit desires. The adolescent boy and girl need to have their attention drawn away from the surging desire of sex and turned in other directions. Freud and his disciples have contributed nothing of value to psychology, and if they have contributed anything to medicine, it is rather discreditable to medicine to have been so far behind the progress of psychology that it could profit by this mixture of psychology and superstition."

Dunlap who has investigated spiritualism in detail finds not a single case in which the claims can be proved or are free from flaws. His discussion is rather of the mental make-up of those who interest themselves in this pastime.

So-called character analysis has developed from the old phrenology, has no scientific basis whatever, and is practically without exception exploited for commercial purposes.

In the psychology of the comic, Dr. Dunlap classifies those things that we term "funny" in various grades from the lowest, the pleasure and amusement that the brute and the savage take in torture, up through horseplay, practical joking, puns, and so on to the idle wittiness. After telling us why we consider these things funny he then offers an explanation as to why we laugh.

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*Thomas Sydenham**

SYDENHAM, like his follower Boerhaave and like Sir James MacKenzie, our modern Sydenham, had little patience with experimental medicine in so far as it had developed during his day, but possessed a clinical acumen that has scarcely been equalled by any other physician and has been excelled only by Hippocrates himself. Dr. Riesman's

*The Sydenham, Clinician. By David Riesman, M.D., Professor of Clinical Medicine, University of Pennsylvania. 46 pages. Paul B. Hoeber, Inc., N. Y. 1926.

presentation of this remarkable man gives us the picture of a very human individual, dictatorial, impatient, and yet conscious of his own mistakes and shortcomings. The small volume provides a most enjoyable half hour.

*Examination of the Patient and Symptomatic Diagnosis**

IN ATTEMPTING to arrive at a diagnosis of a patient's illness, the more thorough the history obtained the greater will be the number of symptoms both past and present which will be utilizable in reaching a conclusion. The symptoms having been discovered, turn now to a stardard work on medicine and you will find that diseases, not symptoms, form the basis of classification. It may then be necessary to search through the description of many diseases before discovering that into which the particular symptomatology under consideration fits completely. Dr. Murray has in his volume roughly reversed this procedure in that he takes up subjective and objective symptoms and under each symptom heading he enumerates the possible etiologic factors, pointing out at the same time what additional or confirmatory questions should be asked or examinations made in order to reach a correct conclusion.

The Peaks of Medical History†

ONE cannot obtain too extensive a historical background for the subject which is one's life work. Dr. Dana touches only the high spots but in doing so he marshals a galaxy of names all of which should be familiar to every student of medicine. In a book the size of this, much of interest must be omitted, and in perusing the very readable pages, one has the feeling that he is witnessing a rapidly moving panorama and regrets his inability to stop here and there and develop a more personal acquaintance with many of the actors as they slip by.

The work might be described as a beginner's history. As such it whets the appetite for more. This was obviously the author's intention for in an appendix entitled Bibliographical Notes he directs the reader to those works carrying greater detail.

But even one who has a fairly general knowledge of medical history will enjoy reading Dana's volume for no two such works are entirely alike, and here and there in the pages one picks up curious and interesting bits of new information.

The illustrations are excellent and numerous. In addition to portraits of the great leaders and thinkers, there are many which indicate medical activities in the different epochs which, as the author states, are kinetic rather than static in their character.

The craftsmanship of the book, as is usually the case with this publisher, is excellent.

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*Examination of the Patient and Symptomatic Diagnosis. By John Watts Murray, M.D. 216 Illustrations. Cloth. Pp. 841. C. V. Mosby Company, St. Louis, Mo. 1926.

†The Peaks of Medical History. (An Outline of the Evolution of Medicine for the use of Medical Students and Practitioners). By Charles L. Dana, A.M., M.D., LL.D., Professor of Nervous Diseases, Cornell University Medical School, Late President of the N. Y. Academy of Medicine. Illustrated with 40 full page plates and 16 test illustrations. Cloth. Pp. 105. Paul B. Hoeber, Inc. New York, 1926.

The Journal of Laboratory and Clinical Medicine

VOL. XIII ST. LOUIS, MO., AUGUST, 1928 NO. 11

Editor-in-Chief: WARREN T. VAUGHAN, M.D.
Richmond, Va.

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Entered at the Post Office at St. Louis, Mo., as Second-Class Matter

EDITORIALS

Recent Studies of Measles

THE first mention of measles as a distinct disease is found in the writings of Ahrun, a physician of Alexandria in 610 A.D., although it was not adequately described until the time of Rhazes, 900 A.D., who distinguished it from smallpox. It remained for Sydenham, in 1655, to separate measles from scarlet fever and to draw attention to it as one of the most important of "the diseases of childhood."

Because of its frequency, its importance, and the often serious nature of its sequelae, a great deal of study has been devoted to the evolution of methods for its prophylaxis and control, and until these are satisfactorily achieved, it is of interest to review from time to time the results of studies applicable to the problem.

The etiology of measles is still under discussion.

The diplococcus described by Tunnicliff and her coworkers has been the subject of much study, as a result of which a skin test for susceptibility to measles has been devised[1, 2] and other evidence adduced in support of their contention as to its etiologic relationship.

Cary and Day[3] report the isolation of a similar organism from 98 per cent of throat cultures, 50 per cent of conjunctival cultures, and 33 per cent of blood cultures in early measles with which they were able to produce rashes and febrile reactions in rabbits, while Ferry and Fisher[4] report the preparation of a measle toxin from filtrates of the aerobic, green-producing streptococcus isolated by Ferry from the blood in early measles.

Hibbard and Duval[5] are convinced that the causal agent of measles exists in the circulating blood during the febrile stage, and that it may be propagated in vitro. While they encountered an organism similar to that described by Tunnicliff, they are noncommittal as to its etiologic relationship to the disease, which, indeed, is so far the status of all the organisms as yet isolated in this disease. In a continuation of their work the same authors elicited further evidence suggesting a definite relation of the Tunnicliff diplococcus and measles,[6] although holding a final conclusion sub judice until further investigations shall determine whether an organism or, as suggested by Park[7] and Degwitz,[8] a filtrable virus.

That the problem is one well meriting study is evidenced by the regularity with which the disease appears and the high incidence of susceptibility, a recent survey showing that approximately 90 per cent of males and 95 per cent of females over twenty have had measles.[9]

In the absence of specific information as to the cause and mechanism of the spread of measles, it is more or less generally accepted that, for the present, attempts at its complete eradication are foredoomed to failure and for this reason competent observers[10, 11] suggest a concentration of effort to protect especially children under three years of age, as fully 70 per cent of all measles deaths fall within that age period.

That such a plan is practical, demands no new methods but merely an intensified application of known procedures, and will produce results, is proved by the report of its practical trial in an epidemic at Syracuse during 1926-27 by Ruhland and Silverman.[12]

It is obvious that in the spread of communicable and infectious diseases the unrecognized case is a factor of great importance.

In the interest of early diagnosis Stimson,[13] in a timely and pertinent paper, comments upon the fact that it is not generally recognized that measles may often be predicted with some confidence before the appearance of Koplik spots and that it is highly contagious from one to two days before these pathognomonic signs appear.

He discusses in extenso the symptoms of measles, especially those of the stage of invasion and incubation, listing them, in the order of appearance, as follows:

1. Malaise, with which there may be headache.

2. Fever.

3. Eye signs (twelve hours later): puffiness of the lower lid, perhaps the measles line and the first sign of exanthem on the fauces. In examining a patient with a cold, therefore, one should examine habitually inside the lower eyelids and inside the cheek.

4. Twelve hours later come the three C's: cough, coryza, and conjunctivitis.

5. Twelve hours later appear Koplik's spots.

6. Twelve hours later the rash appears.

As Stimson says, the physician must be ever on the alert to make the earliest possible diagnosis, to *indiriduallly* isolate the patient on the first suspicion, and to protect him from secondary infection.

Only by these means can the incidence, mortality, and sequelae of this very serious disease be at all controlled until more specific procedures are evolved.

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—*R. A. K.*

Skin Sensitivity and the Dick Test in Newborn Infants

THE introduction of the Dick test as a means of detecting those susceptible to scarlet fever has very naturally led to its extensive use in children.

The similarity of the procedure to that used in the study of those susceptible to diphtheria, the fact that scarlatina convalescents not only give a negative Dick test but their serum when added to the toxin neutralizes its action in the skin of a susceptible individual, all justify the common assumption that a negative Dick test indicates a true antitoxic immunity.

Observations by von Groer and Kassowitz[1] upon the immunity to diphtheria in very young infants as indicated by the Schick test and by the demonstration of antitoxin, showed, however, that while the skin of newborn infants, whose blood did not contain antitoxin, reacts to the Schick test in only about one-third of the cases tested (143), this reactive ability was acquired by the skin in all cases by three months of age.

A similar investigation, but concerned with skin sensitivity to the Dick toxin, is reported by Cooke[2]—apparently the first work of this nature to be recorded.

The investigation covers a study of 200 mothers and their infants during the first ten days of life and again from six weeks to three months later.

In the entire group of infants 86 per cent were negative to the largest amount of toxin used (50 STD) and only 1 per cent was positive to the smallest dose (2 STD). When compared with the reactions of the mothers it is seen that:

A. All infants reacting in any degree had mothers whose skins were extremely or moderately sensitive.

B. More than 75 per cent of the infants with reactions had mothers whose skins were very sensitive.

C. When the mothers' tests were negative or only slightly positive, the infants' tests were always negative.

It is of immediate practical importance to determine whether this negative reaction thus commonly encountered in the newborn is due to a lack of skin sensitivity or to the presence of antitoxin presumably transmitted from mother to infant. Cooke's study was extended to include such a determination.

A sufficiently extensive series of mothers' serum was examined to corroborate the conclusions of others that in those reacting to 2 STD toxin, antitoxin was present. Whenever antitoxin was present in the infant's blood, Cook also found it in the mother's, but the reverse was not true so that, at birth, the presence or absence of antitoxin appears to have no relation to the presence or absence of skin reactivity to toxin, since many infants without antitoxin were negative to 50 STD of toxin. When a number of the same infants whose skin sensitivity had been tested at birth were again tested from six weeks to three months later, there was some skin sensitivity to toxin in about one-third, but only a few were sensitive to small amounts, this development of toxin sensitivity occurring mostly in infants of very sensitive mothers.

From these studies Cooke concludes that the skin in the newborn is not usually sensitive to large doses of scarlatinal toxin; that this lack of sensitivity is not due to the presence of antitoxin; and that skin sensitivity to toxin may develop after some weeks, most often, during the first months of life, in a larger proportion of infants who had no antitoxin at birth than in those whose blood contains antitoxin.

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—*R. A. K.*

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THE SEVENTH ANNUAL CONVENTION OF THE AMERICAN SOCIETY OF CLINICAL PATHOLOGISTS

THIS meeting surpassed all the previous ones both in the scientific character of the papers presented, which have always been good, as well as in the opportunities afforded for intimate personal chats among members for the discussion of problems relating to the practice of clinical pathology. Thanks to the excellent arrangements of the local committee at Minneapolis headed by Dr. Charles R. Drake with the valuable assistance of Dr. G. L. Merkert, practically all of the delegates were housed in the same hostelry, the Leamington Hotel. The scientific and commercial exhibits proved highly interesting due to the untiring efforts of Dr. A. C. Broders and Dr. Kano Ikeda. There were a good many present who had never missed a meeting and others who had come for the first time. A wonderful family spirit prevailed; no distinction was made between the younger men who had just joined and the old war horses who were veterans in the movement. Everybody was made to feel at home and companionship reigned.

At each noon and evening meal there was a spontaneous gathering of Fellows at a large round table in the dining room where informal discussions were held on a great variety of subjects pertaining to clinical pathology, both scientific and economic. This unofficial feature formed a delightful part of

the program of our convention and helped to cement the fast friendships that have been formed among our members since the inception of our organization. Practically all the Fellows promised to make all endeavors to see each other again at the next convention, so that they may carry away with them for the rest of the year the stimulus of meeting their fellow workers and the pleasant experiences of their intellectual encounters with their colleagues in the profession.

In another column will be found the minutes of the convention which will give those who were unable to be present, as well as the many friends of the Society who are interested in its welfare, an idea of the program of the meeting, as well as the newly added round table feature to which a pleasant evening, full of delightful encounters and enlightening information, was devoted.

FRANK WILBUR HARTMAN

Detroit, Michigan

President, 1928-1929

Frank Wilbur Hartman was born in 1890. He obtained an A.B. degree from Knox College in 1913; an M.D. degree from the Medical Department of Johns Hopkins University in 1917. For two and one-half years during the

war he was attached to the U. S. Naval Medical School and U. S. Naval Hospital, Washington, D. C., as pathologist and instructor in pathology. Dr. Hartman was a Lieutenant in the Medical Corp of the U. S. Navy. During this time he also had an assistantship at the George Washington University, Washington, D. C.

Following the war Dr. Hartman was for nearly three years Pathologist and Director of Laboratories at the Scott and White Clinic and Hospital and Santa Fe Hospital in Temple, Texas.

Since August, 1922, Dr. Hartman has been Pathologist and Director of Laboratories at the Henry Ford Hospital in Detroit. He is a member of the

Association of Pathologists and Bacteriologists and American Society of Experimental Pathologists, also a member of the Bone Tumor Committee of the American College of Surgeons at the present time.

Chief interests: Relation of phosphorus and sugar metabolism.
Production and study of experimental nephritis.
Primary heart lesions produced by deep x-ray.

JAMES HARVEY BLACK

Dallas, Texas

President-Elect

James Harvey Black, M.D., born in Huntington, West Virginia, March 27, 1884, is the son of a Methodist minister. Moved to Texas at age of twelve years. He received his academic education at Paris High School, Paris, Texas,

and Southwestern University, Georgetown, Texas; graduated in Medicine in 1907 from the Medical Department of Southwestern University. Was successively interne at St. Paul's Sanitarium, 1906-7; Instructor in Bacteriology and Histology, Southwestern University, 1907-8; Professor of Physiology and Bacteriology, id., 1912-15; Dean Southern Methodist University School of Medicine, 1914-15; Professor of Bacteriology and Preventive Medicine, Baylor University, 1915-17 and 1919-20; Professor of Pathology and Bacteriology, id., 1917-19; Professor of Preventive Medicine, id., since 1920.

Dr. Black is a member of the academic fraternity Kappa Alpha and the medical fraternity Theta Kappa Psi. He is a member of the Methodist Church and of the Masonic Fraternity, Dallas Country Club, Dallas University Club, and Town and Gown Club of Dallas. His scientific affiliations are County, State and American Medical Associations; American Society of Bacteriologists; American Microscopical Society; American Association for the Advancement of Science; American Public Health Association.

His chief interest is in Allergy and Immunology.

MINUTES OF THE SEVENTH ANNUAL CONVENTION OF THE AMERICAN SOCIETY OF CLINICAL PATHOLOGISTS, MINNEAPOLIS, MINNESOTA

The proceedings were held in the Leamington Hotel, Minneapolis, Minnesota, June 8, 9, and 11, 1928.

The meeting was called to order Friday, June 8, 1928, at 9 A.M., by the President, Dr. A. H. Sanford. A short business session was held in which the first order of business was the appointment of a Committee on Necrology, as follows: Dr. Philip Hillkowitz, Denver, Colorado, *Chairman*, Dr. Frank W. Hartman, Detroit, Michigan, Dr. Robert A. Keilty, Washington, D. C., and Dr. Chas. C. W. Judd, Washington, D. C., and a Nominating Committee consisting of Dr. A. H. Schade, Toledo, Ohio, *Chairman*, Dr. C. W. Maynard, Pueblo, Colorado, and Dr. Nathan Rosenthal, New York City.

Dr. Charles R. Drake, Chairman on the Committee on Local Arrangements, made several announcements.

Dr. Philip Hillkowitz, Denver, Colorado, proposed an amendment to the By-Laws to read as follows: Article III, Section 2. The annual dues for active and associate members shall be Ten Dollars ($10.00), payable before or on the date of the annual meeting.

There being no further business the regular scientific session of the Society presented the following program:

The Interpretation of the Wassermann Test. By B. Markowitz, M.D., Chicago, Illinois.

Complement Preservative—A Practical Study. By B. W. Rhamy, M.D., Fort Wayne, Indiana.

Both papers were discussed by Dr. H. C. Sweany, Chicago, Dr. J. J. Moore, Chicago, Dr. Wm. G. Exton, Newark, N. J., Dr. F. E. Sondern, New York, Dr. A. H. Schade, Toledo, Ohio, and closed by Dr. B. Markowitz and Dr. B. W. Rhamy.

The Vegetative Nervous System in Epilepsy. By A. M. P. Saunders, M.D., Chicago, Illinois. (No discussion.)

Method for Measuring the Bactericidal Action of Whole Blood Against Gram Positive Cocci. By William Thalhimer, M.D., and Charlotte Colwell, A.B., Milwaukee, Wisconsin. (Discussed by Dr. Robert F. Maul, Denver, Colorado. Discussion closed by Dr. Wm. Thalhimer.)

The Interpretation of Borderline Allergic Reactions. By Warren T. Vaughan, M.D., Richmond, Va. (Discussed by Dr. J. H. Black, Dallas, Texas, Dr. Wm. G. Exton, Newark, and Dr. A. H. Sanford, Rochester, Minn. The discussion was closed by Dr. Warren T. Vaughan.)

Spectrophotometric Analysis of Blood Serum in Normal and Pathologic Conditions. Study II. By Charles Sheard, Ph.D., T. B. Magath, M.D., and A. E. Osterberg, M.D., Rochester, Minnesota, (Discussed by Dr. F. E. Sondern, and Dr. Wm. G. Exton. Discussion closed by Dr. Charles Sheard.)

Session adjourned.

FRIDAY AFTERNOON, JUNE 8, 1928, 2 P.M.

The meeting was called to order by President A. H. Sanford and the scientific program continued.

Some Tissue Culture Studies. By F. A. Hecker, M.D., Ottumwa, Ia. (Discussed by Dr. Wm. Thalhimer, Dr. Charles Sheard, Rochester, Minn., and Dr. Wm. Carpenter MacCarty, Rochester, Minn. Discussion closed by Dr. F. A. Hecker.)

Pathology of the Thyroid Gland. By John W. Gray, M.D., Newark, N. J. (Discussion by Dr. Wm. Carpenter MacCarty, Dr. Philip Hillkowitz, Dr. George T. Caldwell, Dallas, Texas, Dr. Clarence I. Owen, Detroit, and Dr. Robert A. Keilty, Washington, D. C. Discussion closed by Dr. John W. Gray.)

Improvement in Technic and Results Made in Examining Microscopically by the Razor Section Method Two Thousand Malignant Tissues. By B. T. Terry, M.D., Rochester, Minnesota. (No discussion.)

Further Observations with a New Method for Cultivating Tubercle Bacilli; A Comparison with Guinea Pig Inoculation and Petroff's Method. By H. J. Corper, M.D., and Nao Uyei, Ph.D., Denver, Colorado. (Discussed by Dr. Henry C. Sweany, Chicago, Illinois, and Dr. A. H. Sanford. Discussion closed by Dr. H. J. Corper.)

A System of Sputum Analysis for Acid Fast Bacilli. By Henry C. Sweany, M.D., and Asya Stanichenko, A.B., Chicago, Illinois. (Discussed by Dr. E. D. Downing, Woodman, Colorado, Dr. E. R. Mugrage, Denver, Colorado, and Dr. Robert A. Keilty. Discussion closed by Dr. Henry C. Sweany.)

Tuberculous Endometritis. By H. L. Reinhart, M.D., and Robert A. Moore, M.Sc., Columbus, Ohio. (No discussion.)

Session adjourned.

FRIDAY EVENING, JUNE 8, 1928, 7:30 P.M., ROUND TABLE DISCUSSION.

The meeting was called to order by Dr. A. H. Sanford who introduced the first subject for discussion:

The Postmortem Service at the University of Minnesota. By E. T. Bell, M.D., Minneapolis, Minnesota. (Discussed by Dr. Alvin G. Foord, Buffalo, N. Y., Dr. J. J. Moore, Dr. Wm. Carpenter MacCarty, Dr. A. S. Giordano, South Bend, Indiana, Dr. John W. Gray, Newark, Dr. Henry C. Sweany, Dr. E. R. Mugrage, Denver, Dr. Ernest Scott, Columbus, Ohio, Dr. Robert A. Keilty and Dr. M. Pinson Neal, Columbia, Mo. Discussion closed by Dr. E. T. Bell.)

The Young Clinical Pathologist. By W. G. Gamble, Jr., M.D., Charleston, S. C. (Discussed by Dr. Wm. Carpenter MacCarty, Dr. H. J. Corper, Denver, Dr. B. W. Rhamy, Fort Wayne, Indiana, Dr. C. I. Owen, Detroit, Dr. Walter Freeman, Washington, D. C., Dr. F. W. Hartman, Detroit, and Dr. Philip Hillkowitz. Discussion closed by Dr. W. G. Gamble.)

The Hospital Laboratory Director. By J. J. Moore, M.D., Chicago.

The State Laboratory. By B. W. Rhamy, M.D., Fort Wayne, Indiana. (Discussed by Dr. F. E. Sondern, New York, Dr. A. S. Giordano, South Bend, Indiana, Dr. J. J. Moore, Dr. Wm. G. Exton, Dr. Philip Hillkowitz, Dr. W. G. Gamble and closed by Dr. B. W. Rhamy.)

Membership. By J. H. Black, M.D., Dallas, Texas. (Discussed by Dr. Wm. Carpenter MacCarty, Dr. Wm. G. Exton, Dr. C. E. Roderick, Battle Creek, Michigan, Dr. B. W. Rhamy, Dr. F. W. Hartman, Dr. Margaret Warwick, St. Paul, Minnesota, Dr. F. E. Sondern, Dr. John R. Porter, Rockford, Illinois, Dr. H. J. Corper, Dr. A. S. Giordano, Dr. A. H. Schade, Dr. Robert A. Keilty, Dr. Wm. G. Gamble, and Dr. A. H. Sanford.)

Session adjourned.

SATURDAY MORNING, JUNE 9, 1928, 9 A.M.

The meeting was called to order by President A. H. Sanford and the scientific program continued.

Retention of Urinary Constituents after Anastomosis of Urinary Bladder and Intestines. By F. W. Hartman, M.D., Detroit, Michigan. (Discussed by Dr. F. E. Sondern and closed by Dr. F. W. Hartman.)

The General Practitioner and the Early Diagnosis of Cancer. By Wm. Carpenter MacCarty, M.D., Rochester, Minnesota. (Discussed by Dr. E. L. Miloslavich, Dr. J. J. Moore, Dr. John W. Gray, Dr. Robert A. Keilty, Dr. Walter Freeman, Dr. A. S. Giordano, Dr. A. H. Schade, Dr. B. W. Rhamy, Dr. R. E. Myers, Oklahoma City, Okla., Dr. F. H. Lamb, Davenport, Iowa, Dr. T. C. Terry, Rochester, Minnesota and closed by Dr. Wm. Carpenter MacCarty.)

Rabies in Animals. Demonstrations with Lantern Slides and Motion Picture Films. By E. R. Mugrage, M.D., Denver, Colorado. (Discussed by Dr. A. H. Sanford and Dr. W. G. Gamble. Discussion closed by Dr. E. R. Mugrage.)

The Sedimentation Time of the Blood in Jaundice. By Nathan Rosenthal, M.D., M. I. Blowstein, M.D., and M. Rachmilewitz, M.D., New York City. (No discussion.)

Primary Carcinoma of the Fallopian Tubes. By Earnest Scott, M.D., and Margaret Oliver, Columbus, Ohio. (Discussed by Dr. A. S. Giordano, and Dr. C. I. Owen. Closed by Dr. Ernest Scott.)

A New Method of Colorimetry. By Wm. G. Exton, M.D., Newark, N. J. (Discussed by Dr. Wm. Thalhimer, closed by Dr. Wm. G. Exton.)

The Chemistry and Cytology of Serous Fluids. By Alvin G. Foord, M.D., Guy Youngberg, Ph.D., and Vera Wetmore, B.S., Buffalo, N. Y. (Discussed by Dr. F. E. Sondern, Dr. Kano Ikeda, St. Paul, Minn., and closed by Dr. Alvin G. Foord.)

Value of Nuclear Deviation (Schilling Classification) in Blood Examinations for Clinical Medicine. By F. W. Niehaus, M.D., Omaha, Nebraska. (Discussed by Dr. John W. Gray and Dr. E. R. Mugrage. Closed by Dr. F. W. Niehaus.)

Session adjourned.

SATURDAY AFTERNOON, JUNE 9, 1928, 2 P.M.

The meeting was called to order by President A. H. Sanford and the scientific program continued.

A New Method for Hemoglobin Determinations. By Charles Sheard, Ph.D., and A. H. Sanford, M.D., Rochester, Minnesota.

Pertinent Facts Concerning Hemoglobin. By C. E. Roderick, M.D., Battle Creek, Michigan. Both papers were discussed by Dr. Wm. G. Exton, Dr. A. H. Sanford, Dr. F. E. Sondern, Dr. A. G. Foord and closed by Dr. Charles Sheard.

The Specificity of Bacteria to the Bacteriolytic Action of Chemicals with a Note on this Application to Chemotherapy. By Robert A. Keilty, M.D., Washington, D. C. (Discussed by Dr. Wm. Thalhimer, Dr. C. I. Owen, Dr. F. W. Hartman and closed by Dr. Robert A. Keilty.)

Results in Various Diseases from the Elimination of Foci of Infection and the Use of Vaccine Prepared from Streptococci Having Elective Localizing Power. By E. C. Rosenow, M.D., and A. C. Nickel, M.D., Rochester, Minnesota. (Discussed by Dr. Robert A. Keilty, Dr. F. A. Hecker, and closed by Dr. E. C. Rosenow.)

Further Studies on Brucella Abortus in Man. By A. S. Giordano, M.D., and Marjorie Ableson, South Bend, Indiana. (No discussion.)

The Etiology of Acute Leukemia. By A. S. Rubnitz, M.D., Omaha, Nebraska. (No discussion.)

Examination of Blood for Malaria. By Leon S. Lippincott, M.D., Vicksburg, Mississippi. (No discussion.)

Purpura Hemorrhagica with Report of Three Cases. By Oscar B. Hunter, M.D., Washington, D. C. (Discussed by Dr. John W. Gray.)

Estimating the Increment in Bactericidal Power of Individuals' Blood Produced by Intravenous Injection of Typhoid Vaccine. By Charlotte Colwell, A.B., and J. L. Yates, M.D. (by invitation), Milwaukee, Wisconsin. Read by title.

SATURDAY EVENING, JUNE 9, 1928, 7 P.M., THE ANNUAL BANQUET

The Annual Banquet was held in the ballroom of the Leamington Hotel. The speakers of the evening were as follows:

Presidential Address. By A. H. Sanford, M.D., Rochester, Minn.

The Cults. By Wm. O'Brien, M.D., Minneapolis, Minnesota.

Greetings from the American College of Surgeons. By M. T. MacEachern, M.D., Chicago, Illinois.

Greetings from the American Medical Association. By N. P. Colwell, M.D., Chicago, Illinois.

MONDAY MORNING, JUNE 11, 1928, 9 A.M., THE BUSINESS SESSION

The business session was called to order by President A. H. Sanford.

The reading of the minutes of the previous meeting was dispensed with as they had previously been published.

The Report of the Executive Committee was presented by its Chairman, Dr. John A. Kolmer, Philadelphia. The first matter presented was the question of charging a fee for the registration of technicians, which upon recommendation of the committee was to be deferred until after the report of the Committee on the Registration of Technicians.

The next part of the report was the question of the official organ of the Society. Dr. Kolmer presented tentative articles of agreement with the C. V. Mosby Company, publishers of the JOURNAL OF LABORATORY AND CLINICAL MEDICINE, which the Committee had considered and recommended for adoption by the Society for a two year trial.

The Committee reported that it was decided that the State Laboratory Problem would be submitted with recommendations through the Committee on Public Relations.

The next section of the report of the Executive Committee was the matter of interpreting and amending the By-Laws, if necessary, in relation to Associate Membership in the Society. The Committee reported that in its opinion Section 3 of Article III of the Constitution is satisfactory but recommended special rigorous investigation of each applicant by the Board of Censors, requiring them to accept Article VIII, the Code of Ethics of the By-Laws with the addition of a new section, 4, recommended to the Society for adoption as follows: It shall be deemed unethical for an Associate Member of the Society to assume the independent direction of a laboratory of clinical pathology. A motion was made and carried to accept this recommendation with the addition that Associate Members shall have no vote.

Dr. Kolmer stated that the Executive Committee had examined the books of the Secretary-Treasurer and found them correct.

The entire report of the Executive Committee was accepted by the Society.

The Report of the Committee on Public Relations was given by Dr. F. E. Sondern, New York City. Regarding the State Laboratory question the Committee recommended that a similar committee be continued to make further effort with officials of the American Medical Association, the American College of Surgeons and the American Public Health Association to consider ways and means to correct existing evils through Commissioners of Health, Boards of Supervisors and others who determine the policies of the laboratories under their control.

Relative to the Approval of Laboratories by the American Medical Association, the Committee recommended an endorsement of their efforts in the interest of improving the efficiency of private laboratories. Report accepted. A motion was made and carried that copies of the above resolution be forwarded to the Council on Medical Education and Hospitals of the American Medical Association.

A motion was made and carried that the Committee on Public Relations be instructed to draw up a resolution on behalf of this Society which might go to representa-

tives in different states, that they might use as an argument in favor of presenting this matter to state and county societies; that the matter relative to the resolution be safeguarded by having a referendum adoption by the Executive Committee and then authorization that the Secretary's Office could send copies of this resolution to where it might do some good.

The Report of the Committee on Exhibits was made by Dr. Kano Ikeda, St. Paul, Minnesota, for Dr. A. C. Broders, Chairman, Rochester, Minnesota. The report was accepted by the Society. A motion was made and carried that Exhibits, both scientific and commercial, be handled solely by the Committee on Exhibits of this Society each year.

Dr. John A. Kolmer, Chairman of the Publication Committee reported that that Committee recommends the publication of a book of Approved Clinical Laboratory Methods under the auspices of this Society under the editorship of John A. Kolmer with the assistance and collaboration of a Committee of the Society. Report accepted.

The Report of the Research Committee was presented by Dr. H. J. Corper, Chairman, Denver, Colorado. The Committee recommended the establishment of a yearly Ward Burdick Research Award. Report accepted.

The Report of the Committee on the Registration of Technicians was given by its Chairman, Dr. Kano Ikeda. The report incorporated the establishment of a Registration Bureau for Technicians and was accepted by the Society.

Dr. Philip Hillkowitz, Chairman, presented the report of the Committee on Necrology, telling of the deaths of six members of the Society in the past year, recommending that suitable resolutions of condolence be sent to their respective families. They are, Lieut. Colonel H. J. Nichols, Panama, Dr. Dean N. Beacom, Denver, Colorado, Dr. Reed Rockwood, Baltimore, Maryland, Dr. James C. Todd, Boulder, Colorado, Dr. Ward Burdick, Denver, Colorado, and Dr. Charles E. Simon of Baltimore, Maryland. Report accepted.

The Report of the Committee on Blood Groups was given by its Chairman, Dr. F. W. Hartman, Detroit, recommending the adoption as a Society of the modified Landsteiner classification. Report accepted.

The Report of the Service Bureau Committee was read by Dr. Henry C. Sweany of Chicago, a member of the Committee, in the absence of the Chairman, Dr. Robert A. Kilduffe, Atlantic City, N. J. Report accepted.

Dr. George Ives, Chairman of the Board of Censors, presented the report of the Board. The following were elected to active membership: Dr. H. E. Butka, Los Angeles, Calif., Dr. Ralph A. Fisher, Easton, Pa., Dr. I. A. Nelson, Tulsa, Oklahoma, Dr. Roy W. Hammack, Los Angeles, Dr. John C. Simpson, Norristown, Pa., Dr. Bowman C. Crowell, Chicago, Dr. Wm. McK. Higgins, New York City, Dr. J. Henry Litterer, Nashville, Tenn., Dr. Buist Litterer, Miami, Florida, Dr. Oliver S. Hillman, New York City, Dr. Victor Cefalu, Seattle, Wash., Dr. Marvin D. Bell, Dallas, Texas, Dr. Kenneth Fowler, Danville, Pa., Dr. Louis P. Hastings, Burlington, Vt., Dr. S. Lloyd Johnson, Catonsville, Md., Dr. Mary E. Roche, Norfolk, Va., Dr. J. H. Robinson, Temple, Texas, Dr. Wm. F. Jacobs, Buffalo, N. Y., Dr. P. C. Carson, Denver, Dr. C. J. Bucher, Philadelphia, Dr. Allen C. Nickel, Rochester, Minnesota, Dr. Tomas Cajigas, Washington, D. C., Dr. Walter M. Simpson, Dayton, Ohio, Dr. Sidney C. Dalrymple, Newton Lower Falls, Mass., Dr. Carl H. Reuter, Springfield, Ohio, Dr. E. C. Rosenow, Rochester, Minn., Dr. Wm. Thalhimer, Milwaukee, Wis., Dr. Benjamin S. Kline, Cleveland, Ohio, Dr. George T. Caldwell, Dallas, and Dr. Fred H. Stangl, St. Cloud, Minnesota.

To associate membership: Dr. Fred Boerner, Drexel Hill, Pa., Dr. Israel Davidsohn, Philadelphia, and Dr. Clarence Z. Garber, Detroit, Mich.

Meeting adjourned at 1 P.M.

MONDAY AFTERNOON, JUNE 11, 1928, 2 P.M.

Session called to order by President A. H. Sanford.

Under New Business, Dr. Philip Hillkowitz presented the following amendment to the By-Laws for discussion. Article III, Section 2. The annual dues for active and associate members shall be Ten Dollars ($10.00), payable before or on the date of the annual meeting. A motion was made and carried that the amendment be accepted and become effective with the ensuing year.

A communication from Dr. E. L. Miloslavich, Milwaukee, suggesting a plan for research to be carried out by the Society was read. A motion was made and carried that the matter be referred to the Research Committee.

Dr. F. H. Lamb, Davenport, Iowa, made a motion that the Secretary notify Drs. Sheard and Sanford of our appreciation and thanks for turning over to the American Society of Clinical Pathologists the privilege of exercising control over the commercial production of their new instrument for hemoglobin determinations and that their offer be accepted with gratitude. Motion carried.

It was moved by Dr. Wm. G. Exton that amendments to the Constitution be prepared for presentation next year, whereby the active members shall be hereafter designated as Fellows rather than active members. Motion carried.

A motion was made by Dr. A. H. Schade, Toledo, Ohio, that the Secretary and Board of Censors revise the application blank for membership. Motion carried.

It was moved and carried that a vote of thanks be extended the Local Committee on Arrangements for their great part in the success of the meeting.

The Report of the Nominating Committee was given by the Chairman, Dr. A. H. Schade. The officers elected are as follows:

President, Dr. Frank W. Hartman, Detroit, Michigan.

President-Elect, Dr. J. H. Black, Dallas, Texas.

Vice-President, Dr. Charles E. Drake, Minneapolis, Minnesota.

Secretary-Treasurer, Dr. H. J. Corper, Denver, Colorado.

To Executive Committee, Dr. A. H. Sanford, Rochester, Minnesota, and Dr. John A. Kolmer, Philadelphia, Pennsylvania.

To Board of Censors, Dr. Ernest Scott, Columbus, Ohio, and Dr. B. W. Rhamy, Fort Wayne, Indiana.

President-Elect Frank W. Hartman was escorted to the Chair and the meeting was adjourned at 3 P.M.

Members will kindly report any change in address to the Secretary, Dr. H. J. Corper, Children's Hospital, Denver, Colorado.